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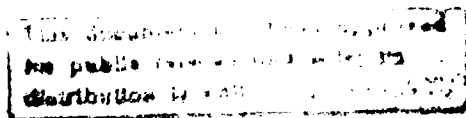
**Acute Intravenous Toxicity Study of
Hypertonic Saline/Dextran 70[®] and its Constituents
in Beagle Dogs**

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**MAMMALIAN TOXICOLOGY BRANCH
DIVISION OF TOXICOLOGY**

June 1989

Toxicology Series: 247



**LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129**

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Acute Intravenous Toxicity Study of Hypertonic Saline/Dextran 70® and its Constituents in Beagle Dogs (Toxicology Series 247)--Frost *et al.*

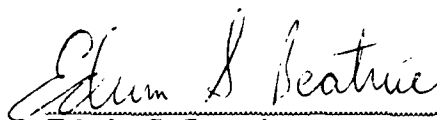
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This research was conducted in compliance with the "Guide for the Care and Use of Laboratory Animals," NIH Publication No. 85-23, as prepared by the Institute of Laboratory Animal Resources, National Research Council.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. (AR 360-5)



Edwin S. Beatrice
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Commanding

19 June 81

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19. ABSTRACT (cont.)

Clinical signs were observed with increased frequency in the HSD and HS-treated groups and included inactivity, tremors, disorientation (HSD only), salivation, vomiting, and thirst. All observed signs dissipated within 24 hours of dosing, with the exception of an occasional incident of diarrhea and one incident of tremors. Significantly increased water consumption was observed on Day 1 in the HSD and HS-treated groups, with a return to control levels by the next day. Significant increases, not associated with visible signs of hemolysis, were observed in aspartate aminotransferase and alkaline phosphatase levels of HSD and D70-treated animals, and in alanine aminotransferase levels of HSD-treated animals when compared to control (RL) and baseline (Day 0) levels. These changes occurred within 6 hours, but were transient, with return to control levels by Days 7 (AST and ALK) or 14 (ALT). Transient elevations of AST and ALT were also observed in HS-treated animals when compared to baseline levels. Other effects on serum chemistry measurements (reductions in albumin, total protein, cholesterol, potassium, calcium, magnesium, iron, blood urea nitrogen, and creatinine 6 hours after infusion with HSD, HS, or D70) could be attributed to transient hemodilution or osmotic diuresis. No other significant changes outside of normal limits were observed in the chemistry data. No significant changes outside of normal limits were observed in the hematology data. Body weights were unaffected by the dosing and no gross or microscopic lesions could be attributed to HSD or its constituents. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings indicate minimal adverse effects should be anticipated with the therapeutic administration of HSD.

ABSTRACT

The acute toxicity following intravenous administration of a proposed resuscitation fluid, hypertonic saline/Dextran 70® (HSD), was evaluated in male and female beagle dogs. Animals received a single intravenous dose of HSD, 20 ml/kg over a 5-minute period, in an attempt to define maximum tolerated dosage. Equal volumes of each HSD component, 7.5% hypertonic saline (HS) and 6% Dextran 70® (D70) in normal saline, and Ringer's lactate (RL) were also evaluated. Blood samples were collected for serum chemistry and hematologic analyses on Day 0 before dosing, at 6, 24, 48, and 72 hours, and Days 7 and 14 after dosing. Observations were made at 1, 2, and 4 hours after administration on the day of dosing and twice daily thereafter. Water consumption was monitored over a 24-hour period weekly during quarantine, daily for the first week of the study, and on Day 14. The animals in each group were euthanized and submitted to necropsy on Day 14 after dosing. Clinical signs were observed with increased frequency in the HSD and HS-treated groups and included inactivity, tremors, disorientation (HSD only), salivation, vomiting, and thirst. All observed signs dissipated within 24 hours of dosing, with the exception of an occasional incident of diarrhea and one incident of tremors. Significantly increased water consumption was observed on Day 1 in the HSD and HS-treated groups, with a return to control levels by the next day. Significant increases, not associated with visible signs of hemolysis, were observed in aspartate aminotransferase and alkaline phosphatase levels of HSD and D70-treated animals, and in alanine aminotransferase levels of HSD-treated animals when compared to control (RL) and baseline (Day 0) levels. These changes occurred within 6 hours, but were transient, with return to control levels by Days 7 (AST and ALK) or 14 (ALT). Transient elevations of AST and ALT were also observed in HS-treated animals when compared to baseline levels. Other effects on serum chemistry measurements (reductions in albumin, total protein, cholesterol, potassium, calcium, magnesium, iron, blood urea nitrogen, and creatinine 6 hours after infusion with HSD, HS, or D70) could be attributed to transient hemodilution or osmotic diuresis. No other significant changes outside of normal limits were observed in the chemistry data. No significant changes outside of normal limits were observed in the hematology data. Body weights were unaffected by the dosing and no gross or microscopic lesions could be attributed to HSD or its constituents. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings indicate minimal adverse effects should be anticipated with the therapeutic administration of HSD.

KEY WORDS

Acute Toxicity, Intravenous Administration, Maximum Tolerated Dose, Hypertonic Saline/Dextran 70®, Hypertonic Saline, Dextran 70®, Ringer's Lactate, Resuscitation Fluid, Beagle Dogs

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PREFACE

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PROJECT/WORK UNIT/APC: 3S463807D836/087/TLRO

GLP STUDY NUMBER: 88003

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DATA MANAGER: Yvonne C. LeTellier, BS

REPORT AND DATA MANAGEMENT: A copy of the final report,
study protocols, retired SOPs,
raw data, analytical and
stability data, and an aliquot
of the test compound will be
retained in the LAIR Archives.

TEST SUBSTANCE: Hypertonic Saline/Dextran 70®

INCLUSIVE STUDY DATES: 13 September 88 - 18 October 88

OBJECTIVE: The objective of this study was to determine
the acute toxicity of hypertonic saline/Dextran
70® following intravenous administration in male
and female beagle dogs.

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**SIGNATURES OF PRINCIPAL SCIENTISTS AND MANAGERS
INVOLVED IN THE STUDY**

We, the undersigned, declare that GLP study number 88003 was performed under our supervision, according to the procedures described herein, and that this report is an accurate record of the results obtained.

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DEPARTMENT OF THE ARMY

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REPLY TO
ATTENTION OF:

SGRD-ULZ-QA

12 June 1989

MEMORANDUM FOR RECORD

SUBJECT: GLP Compliance for GLP Study 88003

1. This is to certify that in relation to LAIR GLP Study 88003 the following inspections were made:

27 January 1988	- Protocol Review
15 September 1988	- Animal Receipt/Room Inspection
22 September 1988	- Randomization
27 September 1988	- Dosing
28 September 1988	- Volumes of Water Bottles
28 September 1988	- Observations/Scoring
28 September 1988	- Hematology
03 October 1988	- Serum Chemistry
04 October 1988	- Weighing
11 October 1988	- Final Sacrifice
14 October 1988	- Test Chemical Log
27 October 1988	- Histology - Tissue Cutting
21 November 1988	- Dextran Analysis in Serum

2. The institute report titled "Acute Intravenous Study of Hypertonic Saline Dextran 70® and its Constituents in Beagle Dogs," Toxicology Series 247, was audited on 5 June 1989.

Carolyn M. Lewis
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Quality Assurance Auditor

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**Acute Intravenous Toxicity Study of Hypertonic
Saline/Dextran 70® and Its Constituents in Beagle
Dogs -- Frost et al.**

INTRODUCTION

During conventional land warfare, it has been estimated that 90% of the deaths occur either in the field or en route to a fixed medical treatment facility and that 50% of those deaths occur due to hemorrhage (1). Conventional treatment of hemorrhage has involved infusion of isotonic resuscitation fluids at volumes equivalent to two or three times the volume of blood lost (2). Supplying this volume of resuscitation fluid on the battlefield for treatment of multiple casualties is not feasible.

Hypertonic crystalloid solutions have been used for the past 70 years in the treatment of hemorrhage (3). However, the consensus has been that unless followed by replacement of the lost blood volume, the beneficial effects of treatment with hyperosmotic solutions are transient (4). Recently, the addition of a hyperoncotic colloid, 6% Dextran 70®, to the hypertonic crystalloid, 7.5% saline, has significantly extended 96-hour survival rates compared with those obtained with normal saline or 7.5% saline (5). Should the effectiveness of this hypertonic saline/Dextran therapy be verified by clinical trial, it would provide a significant advance in the treatment of blood loss due to traumatic injuries.

As with any new treatment regimen, there are potential risks. Low molecular weight dextran could cause bleeding abnormalities and phlebitis or possibly interfere with the cross-matching of blood (6). Hypertonic solutions could cause neurologic abnormalities induced by the rapid increases in osmolalities (7-9) or cardiac arrhythmias induced by the hypokalemia associated with the rapid expansion of extracellular space (2, 10). Consequently, the Division of Toxicology, Letterman Army Institute of Research, was tasked to provide an acute and subchronic toxicity profile of the 7.5% hypertonic saline/6% Dextran 70® resuscitation fluid (HSD). This report describes the results of an acute toxicity study of hypertonic saline/Dextran 70® following intravenous administration of the maximum tolerated dose in male and female beagle dogs.

Objective of Study

The objective of this study was to determine the acute toxicity of hypertonic saline/Dextran 70® following intravenous administration in male and female beagle dogs.

MATERIALS

Test Substance

Name: Hypertonic saline/Dextran 70® (HSD)

LAIR Code NO.: TP96

Lot Number: NC 54845

Expiration Date: September 1989

Composition per 100 ml: Dextran 70® 6 g
 sodium chloride 7.5 g
 water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
 Uppsala, Sweden

Test Substance Constituents

Name: Hypertonic (7.5%) saline (HS)

LAIR Code No.: TP98

Lot Number: I 318712

Expiration Date: 31 December 1988

Composition per 100 ml: sodium chloride 7.5 g
 water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
 Uppsala, Sweden

Name: Dextran 70® (D70)

LAIR Code No.: TP95

Lot Number: NE 54941

Expiration Date: 31 May 1989

Composition per 100 ml: Dextran 70® 6 g
 sodium chloride 0.9 g
 water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
 Uppsala, Sweden

Control

Name: Ringer's lactate (RL)

LAIR Code No.: TP97

Lot Number: NC 54847

Expiration Date: September 1989

Composition per 100 ml: sodium chloride 600 mg
 potassium chloride 30 mg
 calcium chloride
 dihydrate 20 mg
 sodium lactate 310 mg
 water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
 Uppsala, Sweden

Other test substance information is presented in
Appendix A.

Animal Data

Ten male and 10 female beagle dogs (Ridgman Farms, Inc., 301 Main St., Mt. Horeb, WI 53572) were assigned to this study. They were identified individually with the supplier's ear tattoos and corresponding LAIR animal identification numbers. Two male and 2 female dogs were utilized for a preliminary range-finding study and quality control necropsy. The animal weights on receipt (13 September 88) ranged from 7.54 to 10.89 kg. Additional animal data are presented in Appendix B.

Husbandry

Study animals were individually housed in stainless steel runs, which conformed to standards published by the United States Department of Agriculture [Animal Welfare Act (public law 91-579) and DHEW publication No. (NIH) 85-23 (revised, 1985)]. The diet, fed *ad libitum*, consisted of Certified Purina® Canine Diet 5007 (Ralston Purina Company,

St. Louis, MO); water, purified by reverse osmosis, was provided by continuous drip from individual, calibrated, 2-liter cylinders. The animal room temperature and humidity were monitored continuously by hygrothermograph. The temperature was maintained in a range from 15.6°C to 27.2°C. The relative humidity was maintained in a range of 22% to 70% with occasional spikes to as high as 75% during room cleaning. The photoperiod was 12 hours of light per day (0600 - 1800 hours).

METHODS

This study was conducted in accordance with FDA guidelines (11) and LAIR SOP-OP-STX-113, "Acute Intravenous Toxicity Study" (12).

Group Assignment/Acclimation

The animals were randomized into four groups of 2 male and 2 female animals each (Table 1). Allocation was accomplished using a computer-based, stratified, weight-biased method. The XYBION Path/Tox AESLCT Animal Allocation Program was used in conjunction with a VAX 750 Computer.

TABLE 1
Dose Groups

Group	n (each sex)	Solution	Study Termination (Day)
1	2	hypertonic saline/Dextran 70®	14
2	2	hypertonic saline	14
3	2	Dextran 70/normal saline	14
4	2	Ringer's lactate	14

The male and female study animals were acclimated for 13 and 20 days, respectively, before the day of dosing. During this period they were quarantined, examined, and had hematologic and serum chemistry analyses performed in

accordance with LAIR SOP OP-ARG-36 (13). The animals were checked daily for signs of illness and water consumption and body weights were measured weekly.

Dose Levels, Preparation, and Analysis

The maximum tolerated intravenous dose of HSD administered over a 5-minute period was established at 20 ml/kg in preliminary pilot studies. Equal volumes of HS, D70, and RL were administered to animals in the corresponding dose groups. Solutions were used as supplied by the manufacturer, Pharmacia LEO Pharmaceuticals. Analysis of the dosing solutions was provided by Pharmacia LEO Pharmaceuticals. Additional chemical data are presented in Appendix A.

Test Procedures

The acute intravenous toxicity of hypertonic saline/Dextran 70® (HSD) was evaluated in parallel with solutions of its major constituents, hypertonic (7.5%) saline (HS) and Dextran 70® (6%) in normal saline (D70), with Ringer's lactate (RL) serving as the control. The study animals were fed at approximately 0600 on the day of dosing. The dosing solutions were administered between 0830 and 1100 via the cephalic or saphenous veins. Groups were dosed in order of group number, group 1 HSD being first, followed in sequence by group 2 HS, group 3 D70, and group 4 RL. Injections were made using 60 cc syringes (Becton Dickinson & Co., Rutherford, NJ 07070, Lot No. 6K441) and butterfly catheters (Intravenous Injection Set, 19-gage needle-pediatric, disposable type, size 3, Sherwood Medical Co., St. Joseph, MO 64503, Lot No. 517600). Immediately following the injection, a pressure bandage was applied to control any bleeding from the injection site.

Observations

Clinical observations were accomplished 1, 2, and 4 hours after dosing on Day 0, and then at least twice daily for the remainder of the observation period. Body weights were recorded upon receipt of the animals, weekly during the quarantine and observation periods, before dosing, and at necropsy. Water consumption was monitored for a twenty-four hour period, weekly during quarantine, daily for the first week of the study, and at 14 days. Blood samples were collected for serum chemistry and hematologic analyses on Day 0 before dosing, and at 6, 24, 48, and 72 hours and Days 7 and 14 after dosing. Samples for hematology and clotting time determinations were collected in EDTA and citrate tubes,

respectively. All samples for serum chemistry and clotting time determinations were centrifuged within an hour after collection and the serum or plasma frozen at -16°C to -22°C without interruption for a week before analyses.

Necropsy

All animals were submitted for necropsy immediately after receiving a lethal barbiturate overdose. Histopathologic examination was performed on the heart, liver, kidney, brain, lung, spleen, and all gross lesions.

Statistical Analysis

Due to small sample size per sex, males and females were combined for statistical purposes. The means and standard deviations for the body weight, water consumption, serum chemistry, and hematology data for each group were calculated. These data were analyzed using the BMDP statistical software package (14). Each serum chemistry and hematology measurement was subjected to a two-way analysis of covariance using the group's baseline (Day 0) value as the covariate, and dose group and time as the factors of interest. For chemistry and hematology data exhibiting significant group effect or time-group interaction ($p \leq 0.05$) by analysis of covariance, and for all body weight and water consumption data, the equality of the variances for each group was tested using the Levene's test. If equal, the standard one-way analysis of variance was performed for each time period. If unequal, the Welch's one-way analysis of variance was performed for each time period. In either case, if the F-statistic was significant for an analysis of variance for a particular measurement, differences from the control group were evaluated using the Dunnett's test. In addition, the serum chemistry and hematology data of each group were subjected to a separate analysis of variance to determine if significant differences over time occurred. If the F-statistic was significant for this analysis of variance, each time period was compared to the group's baseline value using the Dunnett's test. For total bilirubin, the Kruskal-Wallis nonparametric one-way analysis of variance was performed (14). In addition, Friedman's 2-way ANOVA was used to compare time points for each group. Clinical signs and gross and microscopic pathology findings were described for each animal and tabulated by groups.

Duration of Study

Appendix C is a complete listing of historical events.

Changes/Deviations

The protocol schedule refers to the day of dosing as Day 0. Since XYBION programming refers to the day of dosing as Day 1, a one-day discrepancy exists between the actual study day and day of death listed in the XYBION printouts in Appendix I: Pathology. Day 15 listed in this appendix as the day of death actually refers to study day 14.

It is believed that these changes had no adverse effects on the results of this study.

Storage of Raw Data and Final Report

A copy of the final report, study protocol, raw data, retired SOPs, and an aliquot of the test compounds will be retained in the Letterman Army Institute of Research Archives.

RESULTS

Clinical Observations

The clinical signs observed were grouped into behavioral and gastrointestinal categories. With the exception of 2 cases of diarrhea and 1 case of tremors, all clinical signs were observed on Day 0 following dosing and resolved to normal within 24 hours. Animals receiving HSD or HS exhibited the greatest incidence of signs. No clinical signs were observed in animals receiving Ringer's lactate.

Behavioral signs was the most frequently observed category. Inactivity (9 of 16 animals) was observed in all animals receiving HSD and HS, but only 1 animal receiving D70 was inactive. By four hours after dosing, 1 HSD and 1 HS-treated animal remained inactive. At the next observation period, 24 hours after dosing, all had returned to normal activity levels. Disorientation (6 of 16) was observed in animals receiving HSD (4 animals) and D70 (2 animals). Disorientation resolved by 2 hours in both D70 and 2 HSD-treated animals. At 24 hours after dosing no disorientation was observed. Tremors (6 of 16) were observed in the HS (4 animals) and HSD (2 animals) groups. One animal receiving HS exhibited tremors on Day 1, but the animal returned to normal by Day 2. Ataxia was observed on Day 0 in 1 animal receiving HS.

Gastrointestinal signs observed included vomiting (7 of 16 animals), excessive thirst (2 of 16), increased salivation

(6 of 16), and diarrhea (2 of 16). Vomiting, excessive thirst, and increased salivation were observed only in animals receiving HSD and HS. Diarrhea was observed in 1 animal receiving HS (Days 12-13) and 1 animal receiving D70 (Days 5-6). Diarrhea was not related to the time of dosing.

A summary of clinical observations is presented in Table 2. Individual animal histories are presented in Appendix D.

Body Weights

Animal body weights were not significantly affected by dosing. Group mean body weights are presented in Table 3. Individual animal body weights are presented in Appendix E.

Water Consumption

Group mean water consumption data are presented in Table 4. Individual animal water consumption data are presented in Appendix F. A significant increase in water consumption of approximately 4 times that of the controls was observed on Day 1 ($p = 0.01$) for groups receiving HSD and HS, and on Day 7 ($p = 0.05$) in the group receiving HS.

Serum Chemistry

Group mean serum chemistry data are presented in Table 5. Individual serum chemistry data are presented in Appendix G. Aspartate aminotransferase (AST) levels for animals receiving HSD were significantly increased compared to the controls at 6, 24, 48, and 72 hours ($p = 0.01$) after dosing, with significant increases ($p = 0.05$) compared to the baseline (Day 0) at 6, 24, and 48 hours. Animals receiving D70 also exhibited significantly increased AST levels compared to the controls at 24 hours ($p = 0.05$) and 72 hours ($p = 0.01$). The D70 group exhibited moderately elevated AST levels at 6 and 48 hours, but the differences from the control group were not statistically significant. AST levels were significantly increased compared to the baseline (Day 0) for D70-treated animals at 24, 48, and 72 hours ($p = 0.05$). Compared to the controls, HS-treated animals did not exhibit significant elevations of AST. However, AST levels were significantly increased compared to the baseline (Day 0) for HS-treated animals at 6 hours ($p = 0.05$) after dosing. Alanine aminotransferase (ALT) levels for HSD-treated animals were significantly increased ($p = 0.05$) compared to both the control and baseline levels at 6, 24, 48, and 72 hours. ALT levels for HSD-treated animals were also significantly increased ($p = 0.05$) compared to the controls on Day 7. HS-treated animals also exhibited elevated ALT levels, but the

differences from the controls were not statistically significant. However, ALT levels were significantly increased compared to the baseline (Day 0) for HS-treated animals at 6 and 24 hours ($p = 0.05$). In both HSD and HS-treated animals, the ALT returned to control levels by Day 14. The groups receiving HSD and D70 had significantly elevated alkaline phosphatase (ALK) levels at 6 ($p = 0.01$), 24 ($p = 0.01$), 48 ($p = 0.05$ HSD only), and 72 ($p = 0.01$) hours compared to the controls. ALK levels were significantly increased compared to the baseline (Day 0) for HSD-treated animals at 6, 24, 48, and 72 hours ($p = 0.05$). ALK levels were significantly increased compared to the baseline (Day 0) for D70-treated animals at 24, 48, and 72 hours ($p = 0.05$). The ALK values of HSD and D70-treated groups returned to control levels by Day 7. ALK levels were significantly decreased compared to the baseline (Day 0) for HS-treated animals at 72 hours and 7 days ($p = 0.05$) after dosing. All other statistically significant alterations from control values in serum chemistry measurements occurred at 6 hours, and returned to control levels by 24 hours. At 6 hours, HSD-treated animals exhibited statistically significant reductions in albumin ($p = 0.05$), blood urea nitrogen ($p = 0.01$), and magnesium ($p = 0.01$) levels; HS-treated animals had reduced creatinine ($p = 0.01$) and magnesium ($p = 0.05$) levels; and D70-treated animals exhibited significant reductions in total protein ($p = 0.05$) and cholesterol ($p = 0.05$) levels when compared to controls receiving RL. When each time period was compared to the baseline (Day 0) for each respective group, HSD-treated animals exhibited significant decreases in calcium, cholesterol, albumin, potassium, total protein, creatinine, magnesium and iron levels at 6 hours. With the exception of the magnesium and iron levels, which remained decreased at 24 hours, all measurements returned to baseline by 24 hours after dosing. HSD-treated animals also exhibited a significant ($p = 0.05$) decrease in phosphorus at Day 14. HSD-treated animals exhibited significantly increased ($p = 0.05$) glucose levels at 48 hours compared to the baseline. HS-treated animals exhibited significantly decreased ($p = 0.05$) potassium, creatinine, and magnesium levels at 6 hours compared to the baseline. For HS-treated animals, potassium and creatinine were also significantly decreased ($p = 0.05$) at Days 7 and 14, respectively, compared to the baselines. HS-treated animals exhibited significantly reduced ($p = 0.05$) sodium and magnesium levels at Day 7 compared to the baseline. Albumin levels of the HS and D70 groups were significantly increased ($p = 0.05$) at Day 14 compared to their respective baselines, as was phosphorus in the HS-treated group at 72 hours. D70-treated animals also exhibited significantly reduced ($p = 0.05$) calcium, cholesterol, and total protein levels at 6 hours compared to

the baseline. For D70-treated animals, total protein was also significantly decreased ($p = 0.05$) at 24 and 48 hours compared to the baseline. The Albumin/Globulin Ratio was significantly ($p = 0.05$) increased in the HSD, HS, and D70 groups at Day 14.

Hematology

Group mean hematology data are presented in Table 6. Individual hematology data are presented in Appendix H. A significant increase ($p = 0.05$) from the baseline value was observed in the total leukocyte count for HS-treated animals at 6 hours after dosing. Significant increases from control values were observed in the neutrophil counts for the HSD ($p = 0.01$), HS ($p = 0.01$), and D70-treated ($p = 0.05$) animals at 6 hours after dosing, and again in HSD-treated animals 48 hours after dosing, but the values remained within generally accepted normal limits. Significant increases ($p = 0.05$) from the baseline values were observed in the neutrophil counts for HS and HSD-treated animals at 6 hours after dosing. A significant decrease ($p = 0.05$) from the baseline value was observed in the neutrophil count for HS-treated animals at 14 days after dosing. Significant ($p = 0.05$) decreases were noted in the eosinophil counts at 6 and 48 hours, and at Days 7 and 14; however, all values remained within normal limits. HSD and HS-treated animals also exhibited lymphocyte counts significantly less ($p = 0.01$) than that of the control group at 6 hours, but these values also remained within normal limits. A significant increase ($p = 0.05$) from the baseline value was observed in the lymphocyte count for HS-treated animals at 7 days after dosing. A significant ($p = 0.05$) increase in Mean Corpuscular Volume and a decrease in Mean Corpuscular Hemoglobin Concentration, both at 6 hours, were observed, but all values remained within normal limits. A significant ($p = 0.05$) increase in the Nucleated Red Blood Cell counts was also observed in the HSD-treated group at Day 14, but was considered to be within normal limits.

Necropsy Findings

Pilot study animals submitted as quality controls were free of disease; therefore, the shipment was deemed acceptable for the study. No gross or microscopic pathological lesions attributable to the test compound or its constituents were reported. The Veterinary Pathologist's report is presented in Appendix I.

DISCUSSION

The acute intravenous toxicity of HSD in dogs was evaluated by dosing the animals with an apparently maximum tolerated dose via the cephalic or saphenous veins. This dose had been established in preliminary studies as 20 ml/kg administered over 5 minutes. The 20 ml/kg dose is five times the proposed therapeutic dose of 4 ml/kg (2). In addition to dosing with HSD, groups of dogs were dosed with equal volumes of HS, D70, or RL.

An equal volume of RL was administered as a control. Since RL is an isotonic solution, it provides a basis to compare the effects of the volume administered. Therefore, differences between the RL group and the HSD, HS, and D70 groups can be attributed to the volume expansion capabilities of the latter groups.

Signs observed with increased incidence in the HSD-treated group included inactivity, vomiting, increased salivation, tremors, disorientation, and excessive thirst. Signs observed with increased incidence in the HS-treated group included inactivity, vomiting, increased salivation, tremors, excessive thirst, and ataxia. The D70-treated animals also exhibited an increased incidence of inactivity and disorientation when compared to the controls. No differences due to sex and no mortalities were observed. With the exception of one case of tremors on Day 1 in an HS-treated animal, and two cases of diarrhea unrelated to dosing, all of the signs were observed on Day 0 following dosing, and all animals returned to normal within 24 hours. The observation that behavioral and gastrointestinal signs occurred primarily in animals receiving HSD and HS suggests that the HS component was responsible for inducing the signs. Signs were most likely due to the transient derangement of serum-tissue osmotic balance. This is consistent with the observation that dextran is well tolerated when administered intravenously at doses up to 40 ml/kg in various animal models (G. Jonsson, Pharmacia Pharmaceuticals AB, personal communication).

Body weights were unaffected by dosing.

A significant increase in water consumption was observed on Day 1 in the HSD and HS-treated animals. This is consistent with the increased water volume required for excretion of the excess NaCl component of these solutions.

Animals receiving HSD exhibited significant elevations of AST, ALT, and ALK compared to the control and baseline levels within 6 hours after infusion. Animals receiving D70

also exhibited significantly elevated ALK and AST values compared to the controls within 6 and 24 hours after infusion, respectively. Significant increases compared to baseline levels of AST and ALK were observed at 24, 48, and 72 hours in D70-treated animals. For HSD and D70-treated groups, the changes were not associated with hemolysis, and the AST and ALK values returned to control levels by Day 7. The ALT levels of HSD-treated animals returned to control group levels by Day 14. ALK levels were unaffected by treatment with HS. However, significant elevations of AST (6 hours) and ALT (6 and 24 hours) compared to baseline levels were noted following HS injection. The elevation of ALT in the HS-treated group was greatest at 6 hours, and exhibited a gradual decline to control levels by Day 14, while the AST returned to control levels within 24 hours. Five hours after the intravenous injection of dextran in mice, deposits of material with staining and solubility characteristics similar to dextran were observed in the intracytoplasmic vacuoles of the liver cells (15). No deposits were observed in the livers of saline-treated controls. Although no vacuolization of liver cells was observed in the dog study, the elevation of hepatic enzymes suggests that the dextran component of HSD did have an effect on canine hepatocytes. Moderate elevations of AST and ALT in HS-treated animals suggests that hypertonic saline also contributed to the hepatic changes induced by HSD. The enzymes' return to control levels by Days 7 (AST and ALK) and 14 (ALT), and the absence of morphologic changes in the liver indicate that the hepatic alteration was transient with no residual effect on function.

Reductions in albumin, total protein, cholesterol, calcium, potassium, magnesium, blood urea nitrogen, and creatinine were observed in serum samples collected 6 hours after infusion with HSD, HS, or D70. With the exception of magnesium, all of these reductions were transient, with return to control levels within 24 hours. Total protein in D70-treated animals returned to baseline levels within 72 hours and magnesium in HSD-treated animals returned to baseline levels within 48 hours. The reductions in albumin, total protein, cholesterol, calcium, potassium, and magnesium can be attributed to hemodilution induced by the hyperosmotic solutions. The reductions in BUN and creatinine are consistent with increased urine output from a combination of increased renal blood flow (16), osmotic diuresis resulting from excess sodium and increased water consumption, and release of atrial natriuretic factor (17).

No significant changes outside of normal limits were observed in the hematology measurements.

No significant treatment-related findings were observed at necropsy 14 days after administration of the fluids or in the histological examination of selected tissues. This suggests that any morphological changes due to the administration of the volume expanders were transient, if any did occur.

These data suggest that the maximum tolerated dose of HSD administered intravenously over a 5-minute period is 20 ml/kg in beagle dogs. The toxicity observed following HSD administration was attributable primarily to the HS component and is an expected physiological response to large volumes of hypertonic saline. Moderate increases in serum hepatic enzyme levels attributable to the dextran component were transient with no residual functional or morphologic effect. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings indicate that there will be minimal adverse effects associated with the therapeutic administration of HSD.

CONCLUSION

The maximum tolerated dose of HSD following acute intravenous administration is 20 ml/kg, and the toxicity associated with the HSD administration is consistent with the administration of large volumes of hypertonic saline and hepatic metabolism of dextran. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings indicate that there will be minimal adverse effects associated with the therapeutic administration of HSD.

TABLE 2
Clinical Observations Summary*

Group Sex Observation	RL		HSD		HS		D70	
	M	F	M	F	M	F	M	F
NORMAL THROUGHOUT	2	2	0	0	0	0	1	0
BEHAVIORAL								
INACTIVE	0	0	2	2	2	2	1	0
DISORIENTED	0	0	2	2	0	0	1	1
TREMORS	0	0	1	1	2	2	0	0
ATAXIA	0	0	0	0	1	0	0	0
GASTROINTESTINAL								
VOMITING	0	0	2	2	1	2	0	0
EXCESSIVE THIRST	0	0	1	0	1	0	0	0
INCREASED SALIVATION	0	0	2	2	0	2	0	0
DIARRHEA	0	0	0	0	1	0	0	1

* Data presented as number of animals exhibiting the sign with 2 animals of each sex per group.

TABLE 3

Group Mean Body Weight (kg)[§]

Group	Day of Study					
	-20	-13 ^{&}	-7	0	7	14
RL	9.0	9.3	10.0	10.1	10.5	10.6
	±0.1	0.1	0.3	0.2	0.3	0.2
	(2)	(4)	(4)	(4)	(4)	(4)
HSD	9.6	9.4	9.7	9.9	10.2	10.5
	±1.3	0.9	0.7	0.8	0.9	0.9
	(2)	(4)	(4)	(4)	(4)	(4)
HS	9.4	10.1	10.1	10.6	10.6	11.3
	±0.6	0.5	0.4	0.5	0.6	0.7
	(2)	(4)	(4)	(4)	(4)	(4)
D70	9.5	10.1	10.3	10.7	10.7	11.1
	±0.6	0.5	0.4	0.4	0.6	0.5
	(2)	(4)	(4)	(4)	(4)	(4)

[§] Data are presented as mean ± standard error of the mean with the number of animals, n, in parentheses.

[&] Day -14 for female study animals.

TABLE 4

Group Mean Water Consumption (ml/day)[§]

Group	Day of Study									
	-11 ^{&}	-5 [@]	1	2	3	4	5	6	7	14
RL	780	594	514	479	566	696	707	702	705	716
	±106	96	83	59	31	102	48	60	95	39
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
HSD	943	699	2019*	658	737	547	806	921	857	725
	±131	208	476	67	93	119	62	151	113	50
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
HS	845	675	1955*	538	621	715	849	1124	1533 [†]	713
	±109	129	210	47	64	155	58	318	261	121
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
D70	1012	775	598	677	611	868	802	890	913	666
	±94	174	134	56	48	205	172	164	238	135
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)

[§] Data are presented as mean ± standard error of the mean with number of animals, n, in parentheses.

[&] Day -12 for the female study animals.

[@] Day -6 for the female study animals.

* Value is significantly different from the control at p = 0.01 using the Dunnett's test.

[†] Value is significantly different from the control at p = 0.05 using the Dunnett's test.

TABLE 5
Serum Chemistry Summary^a

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
					Creatinine (mg/dl)				
RL	0.75 ± 0.10 (4)	0.60 0.08 (4)	0.73 0.21 (4)	0.68 0.13 (4)	0.73 0.05 (4)	0.70 0.14 (4)	0.75 0.13 (4)	0.75 0.13 (4)	0.80 0.14 (4)
HSD	0.73 ± 0.10 (4)	0.65 0.10 (4)	0.68 0.10 (4)	0.55 ^e 0.06 (4)	0.75 0.13 (4)	0.70 0.08 (4)	0.68 0.15 (4)	0.68 0.10 (4)	0.73 0.13 (4)
HS	0.78 ± 0.05 (4)	0.68 0.10 (4)	0.65 0.06 (4)	0.50 ^{e*} 0.00 (4)	0.75 0.06 (4)	0.75 0.06 (4)	0.73 0.05 (4)	0.60 0.08 (4)	0.78 ^e 0.05 (4)
D70	0.68 ± 0.15 (4)	0.60 0.08 (4)	0.70 0.08 (4)	0.65 0.06 (4)	0.80 0.08 (4)	0.70 0.08 (4)	0.73 0.10 (4)	0.73 0.05 (4)	0.80 0.08 (4)

\$ Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

@ value is significantly different from the group baseline (Day 0) at $p = 0.05$ using the Dunnett's test.

* Value is significantly different from the control (RL) at $p = 0.01$ using the Dunnnett's test.

TABLE 5 (cont.)

Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Alanine Aminotransferase (U/l)									
RL	31.60 ±5.71 (4)	33.10 10.04 (4)	30.48 7.10 (4)	32.03 7.77 (4)	31.40 7.79 (4)	30.80 8.40 (4)	31.28 7.37 (4)	29.55 6.07 (4)	31.55 10.25 (4)
HSD	35.55 ±13.67 (4)	34.50 8.75 (4)	29.95 3.52 (4)	236.55 [‡] 167.73 (4)	176.65 [‡] 123.53 (4)	140.65 [‡] 91.81 (4)	120.65 [‡] 76.55 (4)	57.13 [‡] 22.95 (4)	31.33 4.42 (4)
HS	28.78 ±4.95 (4)	35.15 16.18 (4)	34.50 11.63 (4)	177.80 [‡] 99.29 (4)	120.25 [‡] 60.92 (4)	88.40 38.53 (4)	73.28 29.82 (4)	38.08 9.10 (4)	28.60 1.91 (4)
D70	32.05 ±9.27 (4)	31.93 7.08 (4)	30.55 4.03 (4)	28.18 1.93 (4)	30.38 2.22 (4)	32.23 2.67 (4)	34.85 2.38 (4)	28.98 4.79 (4)	28.60 5.54 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[‡] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

[†] Value is significantly different from the control (RL) at p = 0.05 using the Dunnett's test.

TABLE 5 (cont.)

Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Total Protein (g/dl)									
RL	5.30	5.23	5.20	5.10	5.30	5.38	5.38	5.10	5.30
	±0.88 (4)	0.22 (4)	0.34 (4)	0.29 (4)	0.56 (4)	0.56 (4)	0.48 (4)	0.67 (4)	0.53 (4)
HSD	5.55	5.50	5.53	4.78 [§]	5.08	5.28	5.53	5.38	5.20
	±0.66 (4)	0.44 (4)	0.33 (4)	0.42 (4)	0.43 (4)	0.26 (4)	0.28 (4)	0.33 (4)	0.56 (4)
HS	5.65	5.23	5.18	5.23	5.10	5.03	5.25	4.65	5.08
	±0.53 (4)	0.36 (4)	0.26 (4)	0.33 (4)	0.27 (4)	0.42 (4)	0.29 (4)	0.61 (4)	0.30 (4)
D70	5.53	5.30	5.20	4.45 ^{§†}	4.78 [§]	4.75 [§]	5.10	5.08	5.18
	±0.94 (4)	0.29 (4)	0.36 (4)	0.34 (4)	0.39 (4)	0.19 (4)	0.08 (4)	0.05 (4)	0.21 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[§] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

[†] Value is significantly different from the control (RL) at p = 0.05 using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Uric Acid (mg/dl)									
RL	0.15	0.23	0.43	0.45	0.55	0.13	0.48	0.53	0.43
	±0.10 (4)	0.15 (4)	0.43 (4)	0.40 (4)	0.35 (4)	0.10 (4)	0.38 (4)	0.38 (4)	0.26 (4)
HSD	0.28	0.18	0.50	0.45	0.50	0.23	0.53	0.48	0.43
	±0.10 (4)	0.21 (4)	0.42 (4)	0.52 (4)	0.47 (4)	0.10 (4)	0.43 (4)	0.41 (4)	0.31 (4)
HS	0.08	0.05	0.35	0.50	0.40	0.10	0.45	0.43	0.25
	±0.10 (4)	0.10 (4)	0.34 (4)	0.41 (4)	0.46 (4)	0.00 (4)	0.40 (4)	0.43 (4)	0.19 (4)
D70	0.10	0.08	0.48	0.50	0.53	0.15	0.43	0.50	0.23
	±0.08 (4)	0.15 (4)	0.25 (4)	0.41 (4)	0.39 (4)	0.10 (4)	0.36 (4)	0.47 (4)	0.22 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Potassium (Meq/l)									
RL	5.25	5.25	5.33	5.13	4.75	4.93	5.08	4.85	5.05
	±0.41 (4)	0.60 (4)	0.26 (4)	0.46 (4)	0.31 (4)	0.19 (4)	0.36 (4)	0.30 (4)	0.34 (4)
HSD	5.28	5.03	5.20	4.08 [ⓐ]	4.70	4.90	5.03	5.25	4.78
	±0.26 (4)	0.13 (4)	0.22 (4)	0.25 (4)	0.42 (4)	0.22 (4)	0.36 (4)	0.29 (4)	0.25 (4)
HS	5.03	5.20	5.10	4.40 [ⓐ]	4.63	4.93	4.80	4.33 [ⓐ]	4.78
	±0.54 (4)	0.23 (4)	0.35 (4)	0.24 (4)	0.15 (4)	0.54 (4)	0.28 (4)	0.44 (4)	0.37 (4)
D70	5.20	5.00	5.08	4.98	4.85	4.88	4.83	4.90	4.78
	±0.38 (4)	0.12 (4)	0.33 (4)	0.17 (4)	0.31 (4)	0.33 (4)	0.35 (3)	0.14 (4)	0.29 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[ⓐ] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Triglycerides (mg/dl)									
RL	77.8	64.5	51.5	57.3	45.3	49.8	52.5	56.5	35.8
	± 47.4	34.4	22.5	25.8	17.0	12.7	17.5	16.4	9.2
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
HSD	53.3	40.0	64.5	39.3	31.8	43.0	60.0	53.8	48.8
	± 16.8	7.5	13.9	29.7	13.7	12.9	15.2	14.7	12.8
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
HS	50.8	47.3	43.5	57.0	47.5	44.8	46.3	54.0	69.8
	± 7.0	13.3	7.1	16.1	15.3	14.5	10.7	14.0	34.9
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
D70	57.0	39.5	41.0	35.8	32.0	35.8	43.0	42.3	38.3
	± 19.2	14.5	12.2	8.5	8.8	12.4	11.4	18.5	6.6
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)

[§] Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

TABLE 5 (cont.)

Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Aspartate Aminotransferase (U/l)									
RL	29.43 ±8.25 (4)	34.85 12.89 (4)	36.55 3.18 (4)	32.20 7.53 (4)	33.20 9.79 (4)	45.33 30.14 (4)	30.20 5.08 (4)	34.28 7.63 (4)	36.23 4.59 (4)
HSD	29.33 ±7.73 (4)	29.58 5.09 (4)	31.83 3.49 (4)	154.93 ^⓪ * 72.86 (4)	126.78 ^⓪ * 40.24 (4)	106.25 ^⓪ * 17.06 (4)	81.98* 14.46 (4)	32.00 5.44 (4)	36.48 4.43 (4)
HS	27.38 ±5.01 (4)	32.33 5.37 (4)	36.95 4.16 (4)	96.15 ^⓪ 54.22 (4)	36.43 3.18 (4)	30.25 4.03 (4)	31.28 4.11 (4)	32.85 3.01 (4)	36.65 4.19 (4)
D70	27.75 ±2.96 (4)	28.55 4.59 (4)	31.68 5.31 (4)	46.05 6.32 (4)	79.68 ^{⓪†} 4.42 (4)	78.80 ^⓪ 30.25 (4)	84.45 ^{⓪*} 7.17 (4)	28.88 2.22 (4)	31.18 6.33 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

^⓪ Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

* Value is significantly different from the control (RL) at p = 0.01 using the Dunnett's test.

† Value is significantly different from the control (RL) at p = 0.05 using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Blood Urea Nitrogen (mg/dl)									
RL	17.05 ±3.77 (4)	20.00 3.24 (4)	19.25 4.80 (4)	20.05 3.18 (4)	15.80 3.14 (4)	16.78 1.75 (4)	18.73 4.73 (4)	18.35 4.37 (4)	14.40 3.51 (4)
HSD	16.65 ±4.91 (4)	17.25 5.68 (4)	16.28 2.46 (4)	12.45* 4.59 (4)	12.90 3.20 (4)	16.43 4.90 (4)	14.83 1.34 (4)	17.40 6.70 (4)	13.83 1.82 (4)
HS	15.73 ±3.06 (4)	21.25 2.70 (4)	16.65 3.22 (4)	14.98 1.33 (4)	14.13 2.33 (4)	17.30 3.72 (4)	16.48 2.26 (4)	17.78 2.23 (4)	13.80 1.53 (4)
D70	17.58 ±2.01 (4)	17.40 4.59 (4)	17.25 5.26 (4)	20.03 3.23 (4)	15.30 2.51 (4)	20.33 5.12 (4)	17.15 2.11 (4)	16.80 5.41 (4)	15.58 2.76 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

* Value is significantly different from the control (RL) at p = 0.01 using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Creatine Phosphokinase (U/l)									
RL	140.69	364.58	228.05	162.95	236.29	165.98	158.68	208.31	284.34
	±23.77 (4)	389.79 (4)	68.34 (4)	54.09 (4)	153.27 (4)	50.94 (4)	40.06 (4)	62.83 (4)	81.23 (4)
HSD	157.62	140.32	163.83	285.22	199.76	213.83	146.13	238.25	317.03
	±21.55 (4)	28.78 (4)	33.22 (4)	144.91 (4)	64.09 (4)	129.22 (4)	36.77 (4)	116.48 (4)	74.58 (4)
HS	133.46	142.16	205.77	303.08	153.71	139.40	142.93	197.66	204.70
	±13.14 (4)	21.30 (4)	52.37 (4)	145.84 (4)	16.26 (4)	13.39 (4)	30.24 (4)	91.66 (4)	44.32 (4)
D70	157.45	198.72	199.01	150.10	175.54	341.07	175.49	196.84	257.35
	±40.89 (4)	137.80 (4)	27.25 (4)	83.94 (4)	74.72 (4)	358.33 (4)	45.69 (4)	76.61 (4)	89.23 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Total Bilirubin (mg/dl)									
RL	0.00	0.05	0.08	0.06	0.06	0.04	0.01	0.10	0.08
	±0.00 (4)	0.10 (4)	0.08 (4)	0.07 (4)	0.07 (4)	0.04 (4)	0.01 (4)	0.12 (4)	0.02 (4)
HSD	0.00	0.04	0.13	0.08	0.14	0.08	0.07	0.15	0.10
	±0.00 (4)	0.08 (4)	0.18 (4)	0.12 (4)	0.14 (4)	0.15 (4)	0.13 (4)	0.14 (4)	0.11 (4)
HS	0.00	0.00	0.02	0.00	0.04	0.02	0.00	0.02	0.05
	±0.00 (4)	0.00 (4)	0.04 (4)	0.00 (4)	0.03 (4)	0.02 (4)	0.00 (4)	0.03 (4)	0.06 (4)
D70	0.00	0.01	0.04	0.00	0.01	0.02	0.00	0.09	0.01
	±0.00 (4)	0.01 (4)	0.04 (4)	0.01 (4)	0.01 (4)	0.03 (4)	0.00 (4)	0.08 (4)	0.02 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Alkaline Phosphatase (U/l)									
RL	74.43 ±11.37 (4)	79.55 12.61 (4)	73.18 2.86 (4)	69.68 6.88 (4)	71.73 3.75 (4)	138.73 130.65 (4)	64.88 2.61 (4)	65.65 8.47 (4)	65.33 2.16 (4)
HSD	85.98 ±19.03 (4)	91.45 15.80 (4)	87.30 18.79 (4)	159.75 [§] * 22.80 (4)	297.53 [§] * 39.04 (4)	363.53 [§] † 44.76 (4)	348.48 [§] * 16.29 (4)	88.83 15.72 (4)	76.05 13.33 (4)
HS	96.48 ±17.85 (4)	96.83 16.27 (4)	103.73 15.77 (4)	95.03 15.34 (4)	98.20 15.44 (4)	93.25 12.95 (4)	89.48 [§] 13.46 (4)	84.45 [§] 7.47 (4)	91.60 18.20 (4)
D70	87.13 ±19.09 (4)	93.43 24.98 (4)	96.53 33.41 (4)	167.65* 35.69 (4)	323.55 [§] * 59.68 (4)	340.00 [§] 186.34 (4)	381.35 [§] * 120.65 (4)	88.13 31.34 (4)	75.83 27.50 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[§] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

* Value is significantly different from the control (RL) at p = 0.01 using the Dunnett's test.

† Value is significantly different from the control (RL) at p = 0.05 using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary\$

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
					Magnesium (mg/dl)				
RL	1.753 ± 0.231 (4)	1.848 0.321 (4)	1.710 0.115 (4)	1.743 0.177 (4)	1.645 0.175 (4)	1.698 0.069 (4)	1.743 0.117 (4)	1.635 0.168 (4)	1.655 0.183 (4)
HSD	1.615 ± 0.104 (4)	1.618 0.076 (4)	1.705 0.126 (4)	1.318 ^{e*} 0.136 (4)	1.430 ^e 0.168 (4)	1.668 0.157 (4)	1.585 0.049 (4)	1.580 0.153 (4)	1.530 0.198 (4)
HS	1.615 ± 0.147 (4)	1.625 0.107 (4)	1.690 0.191 (4)	1.473 ^{e†} 0.111 (4)	1.503 0.038 (4)	1.655 0.099 (4)	1.555 0.065 (4)	1.428 ^e 0.109 (4)	1.560 0.115 (4)
D70	1.683 ± 0.126 (4)	1.640 0.140 (4)	1.665 0.173 (4)	1.493 0.137 (4)	1.585 0.170 (4)	1.540 0.207 (4)	1.243 0.670 (4)	1.523 0.168 (4)	1.595 0.165 (4)

\$ Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

$\hat{\theta}$ value is significantly different from the group baseline (Day 0) at $p = 0.05$ using the Dunnett's test.

* Value is significantly different from the control (RL) at $p = 0.01$ using the Dunnett's test.

† Value is significantly different from the control (RL) at $p = 0.05$ using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary^a

[illegible]

\$ Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

^c Value is significantly different from the group baseline (Day 0) at $p = 0.05$ using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Cholesterol (mg/dl)									
RL	189.60 ±23.55 (4)	174.03 16.12 (4)	169.78 14.66 (4)	174.33 15.53 (4)	175.00 14.33 (4)	163.70 15.85 (4)	175.65 8.73 (4)	170.43 22.08 (4)	162.90 22.11 (4)
HSD	196.10 ±55.40 (4)	171.90 34.46 (4)	172.78 32.43 (4)	136.93 [‡] 23.10 (4)	153.20 19.50 (4)	161.20 36.00 (4)	175.43 46.02 (4)	168.18 40.56 (4)	153.80 26.74 (4)
HS	193.58 ±31.68 (4)	174.55 24.73 (4)	169.00 16.90 (4)	174.80 8.20 (4)	173.55 16.87 (4)	168.10 20.35 (4)	171.58 21.05 (4)	162.60 54.36 (4)	161.20 11.43 (4)
D70	205.15 ±69.79 (4)	175.95 50.15 (4)	169.60 50.02 (4)	131.18 [‡] 32.65 (4)	152.48 33.60 (4)	163.40 43.93 (4)	167.78 44.38 (4)	161.00 51.58 (4)	161.60 43.00 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[‡] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

[†] Value is significantly different from the control (RL) at p = 0.05 using the Dunnett's test.

TABLE 5 (cont.)
Serum Chemistry Summary^a

[illegible]

§ Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

TABLE 6 (cont.)

Hematology Summary

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Mean Corpuscular Hemoglobin (picograms)									
RL	23.78 ± 0.49 (4)	23.85 1.18 (4)	24.48 1.05 (4)	25.00 1.96 (4)	24.18 1.12 (4)	23.93 0.95 (4)	24.15 1.10 (4)	23.95 0.75 (4)	24.33 1.79 (4)
HSD	22.80 ± 0.45 (4)	23.28 0.34 (4)	23.93 0.29 (4)	23.38 0.49 (4)	23.68 0.15 (4)	23.25 0.64 (4)	23.45 0.70 (4)	23.25 1.08 (4)	23.20 0.35 (4)
HS	22.70 ± 1.07 (4)	23.43 1.23 (4)	23.80 1.07 (4)	23.30 1.03 (4)	23.58 1.02 (4)	23.80 1.04 (4)	23.88 1.00 (4)	23.38 1.40 (4)	23.10 1.64 (4)
D70	23.65 ± 0.93 (4)	24.18 1.44 (4)	24.20 1.28 (4)	24.28 1.24 (4)	24.68 1.50 (4)	24.20 1.21 (4)	24.50 1.36 (4)	24.13 0.50 (4)	23.98 1.23 (4)

\$ Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

TABLE 6 (cont.)

Hematology Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Mean Corpuscular Hemoglobin Concentration (g/dl)									
RL	34.23	34.23	35.00	35.85	34.38	34.55	34.40	34.00	34.43
	±0.68 (4)	0.51 (4)	0.50 (4)	2.70 (4)	0.74 (4)	0.45 (4)	0.81 (4)	0.68 (4)	2.28 (4)
HSD	33.65	34.55	35.15	33.68	34.60	34.20	34.53	34.10	33.93
	±0.13 (4)	0.29 (4)	0.48 (4)	0.89 (4)	0.34 (4)	0.65 (4)	0.87 (4)	1.34 (4)	0.42 (4)
HS	33.38	34.03	34.33	33.13 [ⓐ]	33.85	34.58	34.63	33.65	33.40
	±0.74 (4)	0.21 (4)	0.57 (4)	0.22 (4)	0.24 (4)	0.10 (4)	0.35 (4)	0.90 (4)	0.83 (4)
D70	34.08	34.73	34.40	34.80	35.05	34.50	34.83	34.30	34.00
	±0.70 (4)	0.62 (4)	0.37 (4)	0.98 (4)	0.72 (4)	0.55 (4)	0.89 (4)	0.73 (4)	1.00 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[ⓐ] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

TABLE 6 (cont.)

Hematology Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Reticulocytes (%)									
RL	3.23	3.28	1.68	1.78	1.48	1.50	2.25	1.95	1.18
	± 0.97	0.39	0.53	0.93	0.22	0.82	1.81	1.20	0.53
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
HSD	3.33	3.70	3.15	2.13	1.95	1.80	1.28	2.40	2.38
	± 1.20	2.12	1.64	0.74	0.29	0.98	0.22	1.45	1.26
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
HS	3.15	2.88	2.00	1.85	1.28	1.63	1.65	1.65	2.55
	± 1.29	0.38	0.78	1.06	0.73	1.59	0.74	0.99	0.55
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
D70	2.93	3.40	2.25	1.60	1.50	1.23	1.78	2.80	1.35
	± 1.24	1.20	1.20	0.81	0.63	0.74	1.53	2.49	0.94
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)

[§] Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

TABLE 6 (cont.)

Hematology Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Total Leukocyte Count ($\times 10^3/\mu\text{l}$)									
RL	10.98	16.95	11.85	12.75	12.68	14.03	11.10	12.43	10.88
	± 1.68 (4)	10.97 (4)	2.52 (4)	1.74 (4)	3.65 (4)	5.46 (4)	1.63 (4)	2.31 (4)	1.25 (4)
HSD	12.75	13.38	14.90	16.63	12.00	8.20	13.25	13.68	12.23
	± 2.52 (4)	2.56 (4)	7.64 (4)	7.44 (4)	4.95 (4)	4.09 (4)	5.57 (4)	6.23 (4)	4.02 (4)
HS	12.50	12.20	11.48	15.40 [§]	10.05	10.35	10.25	13.08	10.05
	± 2.05 (4)	2.40 (4)	1.46 (4)	1.28 (4)	1.76 (4)	0.83 (4)	2.43 (4)	2.73 (4)	1.63 (4)
D70	13.55	12.13	11.83	11.65	11.28	12.65	12.10	11.38	10.41
	± 1.64 (4)	3.29 (4)	2.77 (4)	2.53 (4)	3.08 (4)	2.98 (4)	2.78 (4)	1.33 (4)	0.81 (4)

[§] Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

[¶] Value is significantly different from the group baseline (Day 0) at $p = 0.05$ using the Dunnett's test.

TABLE 6 (cont.)

Hematology Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Immature Neutrophils (%)									
RL	0.8	1.8	1.5	0.5	0.3	0.5	0.3	0.3	0.5
	± 1.0	1.7	3.0	0.6	0.5	0.6	0.6	0.5	0.6
	(4)	(4)	(4)	(4)	(4)	(4)	(3)	(4)	(4)
HSD	1.5	1.3	2.8	0.0	0.5	0.0	0.3	0.5	0.3
	± 1.9	1.0	3.2	0.0	0.6	0.0	0.6	0.6	0.5
	(4)	(4)	(4)	(4)	(4)	(4)	(3)	(4)	(4)
HS	0.5	1.0	0.5	0.8	1.0	0.3	1.0	0.8	0.3
	± 0.6	1.4	0.6	0.5	0.8	0.5	1.4	1.0	0.5
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
D70	1.0	1.5	0.8	0.5	0.0	0.5	1.5	1.0	0.5
	± 1.4	1.3	1.0	1.0	0.0	1.0	3.0	0.0	0.6
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)

[§] Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

TABLE 6 (cont.)

Hematology Summary^{\$}

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
				Monocytes (%)					
RL	4.8	5.8	5.3	2.5	3.8	5.0	5.3	3.8	4.3
	± 1.9	2.6	2.6	0.6	1.3	1.4	4.7	2.8	2.2
	(4)	(4)	(4)	(4)	(4)	(4)	(3)	(4)	(4)
HSD	6.8	5.8	5.3	5.0	5.8	5.3	4.7	3.0	5.3
	± 2.9	2.5	1.7	2.9	2.2	2.2	3.5	0.8	2.2
	(4)	(4)	(4)	(4)	(4)	(4)	(3)	(4)	(4)
HS	4.8	4.0	5.5	5.8	5.8	2.8	3.8	2.3	4.8
	± 2.6	2.9	1.7	1.0	3.2	3.2	2.2	1.0	3.3
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)
D70	6.8	6.3	2.5	3.5	5.8	7.3	4.3	3.0	6.8
	± 2.1	3.8	2.4	1.7	0.5	2.8	2.6	1.4	2.9
	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)

^{\$} Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

TABLE 6 (cont.)

Hematology Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Nucleated Red Blood Cells (#/100 WBC)									
RL	1.5	0.8	0.0	0.0	0.3	0.0	0.0	0.5	1.5
	±1.7 (4)	1.0 (4)	0.0 (4)	0.0 (4)	0.5 (4)	0.0 (4)	0.0 (3)	1.0 (4)	1.3 (4)
HSD	0.8	1.5	0.0	0.3	0.8	0.5	0.0	0.3	1.5 [ⓐ]
	±0.5 (4)	1.7 (4)	0.0 (4)	0.5 (4)	1.0 (4)	1.0 (4)	0.0 (3)	0.5 (4)	1.7 (4)
HS	0.5	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.3
	±1.0 (4)	0.5 (4)	0.0 (4)	0.0 (4)	0.0 (4)	0.0 (4)	0.0 (4)	0.0 (4)	0.5 (4)
D70	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.5	0.8
	±1.2 (4)	1.4 (4)	0.0 (4)	0.0 (4)	0.0 (4)	0.0 (4)	0.0 (4)	1.0 (4)	0.5 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[ⓐ] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

TABLE 6 (cont.)

Hematology Summary[§]

Group	Day	Day	Day	Hours	Hours	Hours	Hours	Hours	Hours	Day	Day
	-12/-13	-6/-7	0	6	24	48	72	7	14		
Prothrombin Time (seconds)											
RL	8.45	8.75	8.50	9.23	8.85	8.83	8.45	8.08	9.23		
	±2.41 (4)	1.85 (4)	2.55 (2)	2.36 (4)	2.20 (4)	2.67 (4)	2.41 (4)	2.3 (4)	2.98 (4)		
HSD	8.38	8.00	7.40	7.93	7.08	9.35	7.63	7.83	8.63		
	±0.90 (4)	0.71 (2)	1.07 (4)	1.20 (4)	1.09 (4)	2.60 (4)	1.09 (4)	0.29 (3)	1.43 (4)		
HS	7.15	7.28	6.80	8.28	7.13	7.93	9.30	7.40	8.50		
	±1.62 (4)	1.05 (4)	0.96 (3)	0.41 (4)	0.62 (4)	0.15 (4)	3.82 (4)	1.02 (4)	0.85 (4)		
D70	8.05	6.43	7.53	8.43	7.68	8.75	7.90	7.33	9.90		
	±1.14 (4)	0.81 (3)	0.87 (3)	1.14 (4)	1.76 (4)	1.19 (4)	1.01 (4)	0.62 (4)	2.04 (4)		

[§] Data are presented as the mean \pm the standard deviation with the number of animals, n, in parentheses.

TABLE 6 (cont.)

Hematology Summary[§]

Group	Day -12/-13	Day -6/-7	Day 0	Hours 6	Hours 24	Hours 48	Hours 72	Day 7	Day 14
Activated Partial Thromboplastin Time (seconds)									
RL	14.78 ±1.50 (4)	14.97 1.17 (4)	12.35 0.21 (2)	24.25 16.67 (4)	15.88 4.01 (4)	15.63 1.81 (4)	15.20 2.73 (4)	18.70 5.91 (4)	15.50 1.48 (4)
HSD	14.55 ±0.42 (4)	13.60 0.14 (2)	14.30 3.19 (4)	15.50 2.77 (4)	16.88 6.98 (4)	18.35 1.96 (4)	14.60 3.13 (4)	17.45 6.13 (4)	18.13 3.01 (4)
HS	15.10 ±1.12 (4)	13.90 1.56 (4)	21.97 14.52 (3)	15.50 1.06 (4)	19.10 7.66 (4)	22.88 8.37 (4)	17.60 3.90 (4)	15.48 1.39 (4)	16.30 1.29 (4)
D70	14.88 ±1.04 (4)	14.30 2.35 (3)	13.97 0.25 (3)	17.73 [®] 2.94 (4)	16.30 2.82 (4)	17.00 4.26 (4)	14.25 3.03 (4)	15.73 3.23 (4)	18.13 [®] 3.08 (4)

[§] Data are presented as the mean ± the standard deviation with the number of animals, n, in parentheses.

[®] Value is significantly different from the group baseline (Day 0) at p = 0.05 using the Dunnett's test.

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Appendix A: CHEMICAL DATA



Pharmacia

CERTIFICATE OF ANALYSIS 1988-12-19

Product

6 % DEXTRAN 70 IN 7,5 %
SODIUM CHLORIDE INJECTION

Charge No. NC 54845

Inherent viscosity	27 ml/g
Absorbance (375 nm, 10 mm)	0,006
pH	4,6
Heavy metals	< 5 ppm
Sodium chloride	74,7 g/1000 ml
Dextran 70	60 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

Pharmacia AB
Analytical Chemistry Department*Elisabet Fransson*

Elisabet Fransson

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Sweden	Int +46 18 18 30 00	uppsala	pharmup s	Int +46 18 15 41 35

Appendix A (cont.): CHEMICAL DATA



Pharmacia

CERTIFICATE OF ANALYSIS 1988-12-19

Product

7,5 % SODIUM CHLORIDE

Charge No. I 318712

Identification	passed test
Absorbance	0.000
pH	6.0
Heavy metals	< 5 ppm
Sodium chloride	75,0 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test
Released for biological trials.	

Pharmacia AB
Analytical Chemistry Department

Pharmacia Uppläs 1988

Elisabet Fransson

Elisabet Fransson

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Appendix A (cont.): CHEMICAL DATA



Pharmacia

Certificate of analysis

Name: **MACRODEX 60 mg/ml in Normal saline**

Item No.: 10-4510-00

Lot No.: NE 54941

Test		Result	Tolerance limit	Method
Inherent viscosity	ml/g	26	25 - 28	03700
Colour		0,01	Max. 0.04	03811
pH		4,9	4,0 - 7,0	USP XX p. 968
Heavy metals ppm		< 5	Max. 5	USP XX p. 909
Assay for				
- sodium chloride	g/1000ml	8,88	8,10 - 9,90	02355
- dextran 70	g/1000ml	59	54 - 66	02356
Sterility		Passed test	To pass test	02885
Pyrogens		Passed test	To pass test	02983

The identity is assured through strict adherence to established GMP rules throughout the manufacturing procedures.

Released for sale: 1987-05-25

Pharmacia AB
Quality Control Department

Mats Wiberg
Mats Wiberg

M09

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Appendix A (cont.): CHEMICAL DATA



Pharmacia

CERTIFICATE OF ANALYSIS 1988-12-19

Product

LACTATED RINGER'S INJECTION

Charge No. NC 54847

pH	5,8
Heavy metals	< 5 ppm
Sodium	127 mmol/1000 ml
Potassium	3,91 mmol/1000 ml
Calcium	1,30 mmol/1000 ml
Chloride	105,5 mmol/1000 ml
Lactate	27,2 mmol/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

Pharmacia AB
Analytical Chemistry Department

P 440/1 Pharmacia Upplands 1988

Elisabet Fransson
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Appendix B: ANIMAL DATA

Species: *Canis familiaris*

Strain: Beagle

Source: Ridglan Farms, Inc.
301 Main St.
Mt. Horeb, WI 53572

Sex: Male and Female

Month of birth: Mar 88

Method of randomization: Weight bias, stratified animal allocation (XYBION Medical Systems PATH/TOX AESLCT Program)

Animals in each group: 2 Males and 2 Females

Condition of animals at start of study: Normal

Body weight range at dosing:	Males	7.9 - 11.6 kg
	Females	9.2 - 11.6 kg

Identification procedures: Supplier ear tattoo with corresponding LAIR animal number

Pretest conditioning: Quarantine/acclimation 14 September 1988 to 26 September and 3 October 1988, males and females, respectively

Justification: The beagle dog is a standard laboratory model for acute toxicity studies and is accepted by all regulatory agencies.

Appendix C: HISTORICAL LISTING OF STUDY EVENTS

<u>Date</u>	<u>Event</u>
13 Sep 88	Animals arrived. They were sexed, observed for illness, and caged in the GLP Suite.
14, 26 Sep 88	Pre- and post-quarantine physical examinations were conducted.
14, 20, 27 Sep, 4, 11, 18 Oct 88	Animals were weighed.
14, 21, 22, 27 - 30 Sep, 4 - 7, 11, 18 Oct 88	Blood was taken by venipuncture for hematology and clinical chemistry analyses.
14 Sep - 17 Oct 88	Animals were observed twice daily
22 Sep 88	Animals were randomized into groups.
16, 22, 28 Sep - 11, 18 Oct 88	Water consumption was monitored.
27 Sep, 4 Oct 88	Animals were dosed beginning at approximately 0830 hours. Observations were conducted one, two, and four hours after dosing.
27 Sep - 18 Oct 88	Clinical signs were recorded.
11, 18 Oct 88	Animals were delivered to Necropsy Suite for blood sampling, euthanasia, and necropsy.

Appendix D: INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00032 Sex: Male Group: 1			
27-Sep-88	0	08:28	DOSED
27-Sep-88	0	09:28	VOMITING, SEVERE EXCESSIVE THIRST, SEVERE INACTIVE, MODERATE DISORIENTED, MODERATE INCREASED SALIVATION, SLIGHT TREMORS, SLIGHT
27-Sep-88	0	10:28	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	12:28	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:45	NORMAL/NO SIGNIFICANT SIGNS
29-Sep-88	2	14:12	NORMAL/NO SIGNIFICANT SIGNS
30-Sep-88	3	10:55	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:25	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:17	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:50	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:50	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:20	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:30	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	13	08:30	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	14	06:22	NORMAL, EUTHANIZED
Animal: 88A00028 Sex: Male Group: 1			
27-Sep-88	0	08:43	DOSED
27-Sep-88	0	09:43	INCREASED SALIVATION, SEVERE INACTIVE, SEVERE VOMITING, SEVERE DISORIENTED, MODERATE
27-Sep-88	0	10:43	INACTIVE, SLIGHT
27-Sep-88	0	12:43	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:46	NORMAL/NO SIGNIFICANT SIGNS
29-Sep-88	2	14:15	NORMAL/NO SIGNIFICANT SIGNS
30-Sep-88	3	10:54	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:15	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:16	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:48	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00028 Sex: Male Group: 1			
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:49	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:00	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:15	NCRMAL/NO SIGNIFICANT SIGNS
10-Oct-88	13	08:30	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	14	06:15	NORMAL, EUTHANIZED
Animal: 88A00037 Sex: Male Group: 2			
27-Sep-88	0	10:05	DOSED
27-Sep-88	0	11:05	EXCESSIVE THIRST, SEVERE INACTIVE, SLIGHT
27-Sep-88	0	12:05	INACTIVE, SLIGHT
27-Sep-88	0	14:05	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:55	TREMORS, SLIGHT
29-Sep-88	2	14:15	NORMAL/NO SIGNIFICANT SIGNS
30-Sep-88	3	10:58	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:15	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:27	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:50	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:50	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:22	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:30	DIARRHEA, MODERATE
10-Oct-88	13	08:30	DIARRHEA, SLIGHT
11-Oct-88	14	06:32	NORMAL, EUTHANIZED
Animal: 88A00035 Sex: Male Group: 2			
27-Sep-88	0	09:57	DOSED
27-Sep-88	0	10:57	VOMITING, MODERATE INACTIVE, MODERATE ATAxia, SLIGHT TREMORS, SLIGHT
27-Sep-88	0	11:57	INACTIVE, SLIGHT ATAxia, SLIGHT TREMORS, SLIGHT
27-Sep-88	0	13:57	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:50	NORMAL/NO SIGNIFICANT SIGNS
29-Sep-88	2	14:15	NORMAL/NO SIGNIFICANT SIGNS

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00035 Sex: Male Group: 2			
30-Sep-88	3	10:57	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:15	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:20	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:50	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:50	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:21	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:30	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	13	08:30	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	14	06:29	NORMAL, EUTHANIZED
Animal: 88A00033 Sex: Male Group: 3			
27-Sep-88	0	10:20	DOSED
27-Sep-88	0	11:20	INACTIVE, SLIGHT DISORIENTED, MODERATE
27-Sep-88	0	12:20	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	14:20	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:47	NORMAL/NO SIGNIFICANT SIGNS
29-Sep-88	2	14:15	NORMAL/NO SIGNIFICANT SIGNS
30-Sep-88	3	10:56	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:15	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:18	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:50	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:50	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:21	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:30	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	13	08:30	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	14	06:24	NORMAL, EUTHANIZED
Animal: 88A00031 Sex: Male Group: 3			
27-Sep-88	0	10:35	DOSED
27-Sep-88	0	11:35	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	12:35	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	14:35	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:44	NORMAL/NO SIGNIFICANT SIGNS

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00031 Sex: Male Group: 3			
29-Sep-88	2	14:15	NORMAL/NO SIGNIFICANT SIGNS
30-Sep-88	3	10:55	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:15	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:16	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:50	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:50	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:20	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:30	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	13	08:30	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	14	06:19	NORMAL, EUTHANIZED
Animal: 88A00034 Sex: Male Group: 4			
27-Sep-88	0	10:55	DOSED
27-Sep-88	0	11:55	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	12:55	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	14:55	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:49	NORMAL/NO SIGNIFICANT SIGNS
29-Sep-88	2	14:15	NORMAL/NO SIGNIFICANT SIGNS
30-Sep-88	3	10:56	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:15	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:19	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:50	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:50	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:21	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:30	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	13	08:30	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	14	06:26	NORMAL, EUTHANIZED
Animal: 88A00029 Sex: Male Group: 4			
27-Sep-88	0	11:08	DOSED
27-Sep-88	0	12:08	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	13:08	NORMAL/NO SIGNIFICANT SIGNS
27-Sep-88	0	15:08	NORMAL/NO SIGNIFICANT SIGNS
28-Sep-88	1	10:42	NORMAL/NO SIGNIFICANT SIGNS

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00029 Sex: Male Group: 4			
29-Sep-88	2	14:15	NORMAL/NO SIGNIFICANT SIGNS
30-Sep-88	3	10:54	NORMAL/NO SIGNIFICANT SIGNS
01-Oct-88	4	10:15	NORMAL/NO SIGNIFICANT SIGNS
02-Oct-88	5	09:00	NORMAL/NO SIGNIFICANT SIGNS
03-Oct-88	6	14:15	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	7	14:48	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	8	09:00	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	9	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	10	13:50	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	11	08:20	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	12	08:30	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	13	08:30	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	14	06:17	NORMAL, EUTHANIZED
Animal: 88A00043 Sex: Female Group: 1			
04-Oct-88	0	08:27	DOSED
04-Oct-88	0	09:27	INACTIVE, MODERATE INCREASED SALIVATION, MODERATE VOMITING, MODERATE TREMORS, SLIGHT
04-Oct-88	0	10:27	INACTIVE, SLIGHT TREMORS, SLIGHT DISORIENTED, MODERATE
04-Oct-88	0	12:27	DISORIENTED, SLIGHT
05-Oct-88	1	09:40	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	2	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	3	14:00	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	4	08:30	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	5	08:15	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	6	08:40	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	7	08:28	NORMAL/NO SIGNIFICANT SIGNS
12-Oct-88	8	07:47	NORMAL/NO SIGNIFICANT SIGNS
13-Oct-88	9	09:00	NORMAL/NO SIGNIFICANT SIGNS
14-Oct-88	10	13:30	NORMAL/NO SIGNIFICANT SIGNS
15-Oct-88	11	08:22	NORMAL/NO SIGNIFICANT SIGNS
16-Oct-88	12	08:43	NORMAL/NO SIGNIFICANT SIGNS
17-Oct-88	13	14:30	NORMAL/NO SIGNIFICANT SIGNS
18-Oct-88	14	07:15	NORMAL, EUTHANIZED

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00047 Sex: Female Group: 1			
04-Oct-88	0	08:42	DOSED
04-Oct-88	0	09:42	INCREASED SALIVATION, MODERATE INACTIVE, SEVERE VOMITING, SEVERE DISORIENTED, MODERATE
04-Oct-88	0	10:42	INACTIVE, SEVERE VOMITING, SLIGHT DISORIENTED, MODERATE
04-Oct-88	0	12:42	INACTIVE, SLIGHT DISORIENTED, MODERATE
05-Oct-88	1	09:42	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	2	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	3	14:00	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	4	08:30	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	5	08:15	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	6	08:40	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	7	08:33	NORMAL/NO SIGNIFICANT SIGNS
12-Oct-88	8	08:51	NORMAL/NO SIGNIFICANT SIGNS
13-Oct-88	9	09:00	NORMAL/NO SIGNIFICANT SIGNS
14-Oct-88	10	13:30	NORMAL/NO SIGNIFICANT SIGNS
15-Oct-88	11	08:27	NORMAL/NO SIGNIFICANT SIGNS
16-Oct-88	12	08:55	NORMAL/NO SIGNIFICANT SIGNS
17-Oct-88	13	14:30	NORMAL/NO SIGNIFICANT SIGNS
18-Oct-88	14	07:15	NORMAL, EUTHANIZED
Animal: 88A00044 Sex: Female Group: 2			
04-Oct-88	0	08:58	DOSED
04-Oct-88	0	09:58	VOMITING, SEVERE INCREASED SALIVATION, SEVERE INACTIVE, MODERATE TREMORS, SLIGHT
04-Oct-88	0	10:58	VOMITING, SLIGHT INACTIVE, MODERATE
04-Oct-88	0	12:58	INACTIVE, SLIGHT
05-Oct-88	1	09:47	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	2	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	3	14:00	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	4	08:30	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	5	08:15	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	6	08:40	NORMAL/NO SIGNIFICANT SIGNS

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00044 Sex: Female Group: 2			
11-Oct-88	7	08:29	NORMAL/NO SIGNIFICANT SIGNS
12-Oct-88	8	07:50	NORMAL/NO SIGNIFICANT SIGNS
13-Oct-88	9	09:00	NORMAL/NO SIGNIFICANT SIGNS
14-Oct-88	10	13:30	NORMAL/NO SIGNIFICANT SIGNS
15-Oct-88	11	08:23	NORMAL/NO SIGNIFICANT SIGNS
16-Oct-88	12	08:43	NORMAL/NO SIGNIFICANT SIGNS
17-Oct-88	13	14:30	NORMAL/NO SIGNIFICANT SIGNS
18-Oct-88	14	07:15	NORMAL, EUTHANIZED
Animal: 88A00042 Sex: Female Group: 2			
04-Oct-88	0	09:10	DOSED
04-Oct-88	0	10:10	VOMITING, MODERATE INACTIVE, SEVERE INCREASED SALIVATION, SEVERE TREMORS, MODERATE
04-Oct-88	0	11:10	INACTIVE, MODERATE INCREASED SALIVATION, SLIGHT TREMORS, SLIGHT
04-Oct-88	0	13:10	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	1	09:48	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	2	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	3	14:00	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	4	08:30	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	5	08:15	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	6	08:40	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	7	08:28	NORMAL/NO SIGNIFICANT SIGNS
12-Oct-88	8	07:46	NORMAL/NO SIGNIFICANT SIGNS
13-Oct-88	9	09:00	NORMAL/NO SIGNIFICANT SIGNS
14-Oct-88	10	13:30	NORMAL/NO SIGNIFICANT SIGNS
15-Oct-88	11	08:23	NORMAL/NO SIGNIFICANT SIGNS
16-Oct-88	12	08:43	NORMAL/NO SIGNIFICANT SIGNS
17-Oct-88	13	14:30	NORMAL/NO SIGNIFICANT SIGNS
18-Oct-88	14	07:15	NORMAL, EUTHANIZED
Animal: 88A00040 Sex: Female Group: 3			
04-Oct-88	0	09:25	DOSED
04-Oct-88	0	10:25	DISORIENTED, SLIGHT
04-Oct-88	0	11:25	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	0	13:25	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	1	09:49	NORMAL/NO SIGNIFICANT SIGNS

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments		
Animal: 88A00040 Sex: Female Group: 3					
06-Oct-88	2	13:00	NORMAL/NO	SIGNIFICANT	SIGNS
07-Oct-88	3	14:00	NORMAL/NO	SIGNIFICANT	SIGNS
08-Oct-88	4	08:30	NORMAL/NO	SIGNIFICANT	SIGNS
09-Oct-88	5	08:15	NORMAL/NO	SIGNIFICANT	SIGNS
10-Oct-88	6	08:40	NORMAL/NO	SIGNIFICANT	SIGNS
11-Oct-88	7	08:26	NORMAL/NO	SIGNIFICANT	SIGNS
12-Oct-88	8	07:45	NORMAL/NO	SIGNIFICANT	SIGNS
13-Oct-88	9	09:00	NORMAL/NO	SIGNIFICANT	SIGNS
14-Oct-88	10	13:30	NORMAL/NO	SIGNIFICANT	SIGNS
15-Oct-88	11	08:21	NORMAL/NO	SIGNIFICANT	SIGNS
16-Oct-88	12	08:42	NORMAL/NO	SIGNIFICANT	SIGNS
17-Oct-88	13	14:30	NORMAL/NO	SIGNIFICANT	SIGNS
18-Oct-88	14	07:15	NORMAL, EUTHANIZED		
Animal: 88A00046 Sex: Female Group: 3					
04-Oct-88	0	09:36	DOSED		
04-Oct-88	0	10:36	NORMAL/NO	SIGNIFICANT	SIGNS
04-Oct-88	0	11:36	NORMAL/NO	SIGNIFICANT	SIGNS
04-Oct-88	0	13:36	NORMAL/NO	SIGNIFICANT	SIGNS
05-Oct-88	1	09:50	NORMAL/NO	SIGNIFICANT	SIGNS
06-Oct-88	2	13:00	NORMAL/NO	SIGNIFICANT	SIGNS
07-Oct-88	3	14:00	NORMAL/NO	SIGNIFICANT	SIGNS
08-Oct-88	4	08:30	NORMAL/NO	SIGNIFICANT	SIGNS
09-Oct-88	5	08:15	DIARRHEA, MODERATE		
10-Oct-88	6	08:40	DIARRHEA, SLIGHT		
11-Oct-88	7	08:32	NORMAL/NO	SIGNIFICANT	SIGNS
12-Oct-88	8	07:50	NORMAL/NO	SIGNIFICANT	SIGNS
13-Oct-88	9	09:00	NORMAL/NO	SIGNIFICANT	SIGNS
14-Oct-88	10	13:30	NORMAL/NO	SIGNIFICANT	SIGNS
15-Oct-88	11	08:26	NORMAL/NO	SIGNIFICANT	SIGNS
16-Oct-88	12	08:54	NORMAL/NO	SIGNIFICANT	SIGNS
17-Oct-88	13	14:30	NORMAL/NO	SIGNIFICANT	SIGNS
18-Oct-88	14	07:20	NORMAL, EUTHANIZED		
Animal: 88A00038 Sex: Female Group: 4					
04-Oct-88	0	09:47	DOSED		
04-Oct-88	0	10:47	NORMAL/NO	SIGNIFICANT	SIGNS
04-Oct-88	0	11:47	NORMAL/NO	SIGNIFICANT	SIGNS
04-Oct-88	0	13:47	NORMAL/NO	SIGNIFICANT	SIGNS

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

Date	Day of Study	Time of Day	Observations and Comments
Animal: 88A00038 Sex: Female Group: 4			
05-Oct-88	1	09:50	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	2	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	3	14:00	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	4	08:30	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	5	08:15	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	6	08:40	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	7	08:24	NORMAL/NO SIGNIFICANT SIGNS
12-Oct-88	8	07:45	NORMAL/NO SIGNIFICANT SIGNS
13-Oct-88	9	09:00	NORMAL/NO SIGNIFICANT SIGNS
14-Oct-88	10	13:30	NORMAL/NO SIGNIFICANT SIGNS
15-Oct-88	11	08:20	NORMAL/NO SIGNIFICANT SIGNS
16-Oct-88	12	08:42	NORMAL/NO SIGNIFICANT SIGNS
17-Oct-88	13	14:30	NORMAL/NO SIGNIFICANT SIGNS
18-Oct-88	14	07:09	NORMAL, EUTHANIZED
Animal: 88A00041 Sex: Female Group: 4			
04-Oct-88	0	09:56	DOSED
04-Oct-88	0	10:56	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	0	11:56	NORMAL/NO SIGNIFICANT SIGNS
04-Oct-88	0	13:56	NORMAL/NO SIGNIFICANT SIGNS
05-Oct-88	1	09:51	NORMAL/NO SIGNIFICANT SIGNS
06-Oct-88	2	13:00	NORMAL/NO SIGNIFICANT SIGNS
07-Oct-88	3	14:00	NORMAL/NO SIGNIFICANT SIGNS
08-Oct-88	4	08:30	NORMAL/NO SIGNIFICANT SIGNS
09-Oct-88	5	08:15	NORMAL/NO SIGNIFICANT SIGNS
10-Oct-88	6	not rec.	NORMAL/NO SIGNIFICANT SIGNS
11-Oct-88	7	08:27	NORMAL/NO SIGNIFICANT SIGNS
12-Oct-88	8	07:45	NORMAL/NO SIGNIFICANT SIGNS
13-Oct-88	9	09:00	NORMAL/NO SIGNIFICANT SIGNS
14-Oct-88	10	13:30	NORMAL/NO SIGNIFICANT SIGNS
15-Oct-88	11	08:27	NORMAL/NO SIGNIFICANT SIGNS
16-Oct-88	12	08:42	NORMAL/NO SIGNIFICANT SIGNS
17-Oct-88	13	14:30	NORMAL/NO SIGNIFICANT SIGNS
18-Oct-88	14	07:15	NORMAL, EUTHANIZED

Appendix E: BODY WEIGHTS (kg)

Animal	Day of Study					
	-20	-13*	-7	0	7	14
88A000-						
RL Male and Female						
29		9.5	10.7	10.5	11.0	11.0
34		9.0	9.2	9.6	9.6	9.9
38	9.1	9.6	10.3	10.1	10.6	10.6
41	8.9	9.2	9.6	10.0	10.6	10.8
Mean	9.0	9.3	10.0	10.1	10.5	10.6
Std.Dev	0.1	0.3	0.7	0.4	0.6	0.5
SEM	0.1	0.1	0.3	0.2	0.3	0.2
HSD Male and Female						
28		7.5	8.3	7.9	8.2	8.6
32		10.5	10.5	11.0	11.4	12.0
43	8.3	8.4	8.7	9.2	9.3	9.2
47	10.9	11.2	11.2	11.6	12.0	12.1
Mean	9.6	9.4	9.7	9.9	10.2	10.5
Std.Dev	1.8	1.7	1.4	1.7	1.8	1.8
SEM	1.3	0.9	0.7	0.8	0.9	0.9

* Day -14 for the female study animals.

Appendix E (cont.): BODY WEIGHTS (kg)

Animal	Day of Study					
	-20	-13*	-7	0	7	14
88A000-						
HS Male and Female						
35		10.9	11.0	11.6	11.9	12.5
37		10.6	10.1	11.0	11.4	12.0
42	10.0	10.2	10.2	10.6	9.6	11.2
44	8.8	8.8	8.9	9.3	9.6	9.5
Mean	9.4	10.1	10.1	10.6	10.6	11.3
Std.Dev	0.8	0.9	0.9	1.0	1.2	1.3
SEM	0.6	0.5	0.4	0.5	0.6	0.7
D70 Male and Female						
31		9.3	10.3	10.1	10.5	10.8
33		10.7	10.5	11.4	11.4	11.5
40	8.9	9.2	9.4	9.8	9.1	9.8
46	10.1	11.1	11.1	11.5	11.9	12.1
Mean	9.5	10.1	10.3	10.7	10.7	11.1
Std.Dev	0.8	1.0	0.7	0.9	1.2	1.0
SEM	0.6	0.5	0.4	0.4	0.6	0.5

* Day -14 for the female study animals.

Appendix F: WATER CONSUMPTION (ml/day)

Animal	Day of Study									
	-11*	-5 [@]	1	2	3	4	5	6	7	14
<hr/>										
RL Male and Female										
29	995	380	672	555	586	455	582	883	740	662
34	900	700	284	584	484	600	682	653	435	812
38	710	493	520	324	560	880	768	637	876	645
41	516	802	578	454	632	848	795	635	768	745
<hr/>										
Mean	780	594	514	479	566	696	707	702	705	716
Std.Dev	212	192	165	118	62	204	96	121	189	77
SEM	106	96	83	59	31	102	48	60	95	39
<hr/>										
HSD Male and Female										
28	730	640	1554	610	948	720	752	778	541	795
32	1290	300	978	715	496	195	752	1370	1030	700
43	750	571	2393	498	722	617	728	730	849	595
47	1000	1283	3152	810	780	657	990	805	1008	810
<hr/>										
Mean	943	699	2019	658	737	547	806	921	857	725
Std.Dev	262	416	953	134	187	239	124	301	226	99
SEM	131	208	476	67	93	119	62	151	113	50

* Day -12 for the female study animals.

[@] Day -6 for the female study animals.

Appendix F (cont.): WATER CONSUMPTION (ml/day)

Animal	Day of Study									
	-11*	-5 [@]	1	2	3	4	5	6	7	14
<hr/>										
HS Male and Female										
35	1033	455	1418	602	437	430	792	1241	1980	980
37	788	1000	2437	399	730	495	730	1978	1990	763
42	1000	764	1929	576	646	1092	997	635	1078	715
44	560	481	2037	575	672	842	877	643	1084	395
<hr/>										
Mean	846	675	1955	538	621	715	849	1124	1533	713
Std.Dev	219	258	420	94	128	310	116	636	522	241
SEM	109	129	210	47	64	155	58	318	261	121
<hr/>										
D70 Male and Female										
31	1255	570	574	671	486	755	647	530	740	525
33	998	720	330	525	636	575	732	1085	1290	479
40	795	528	521	727	605	667	525	706	318	595
46	1000	1283	967	785	718	1474	1303	1237	1302	1065
<hr/>										
Mean	1012	775	598	677	611	868	802	890	913	666
Std.Dev	188	348	267	112	96	411	345	328	475	270
SEM	94	174	134	56	48	205	172	164	238	135

* Day -12 for the female study animals.

[@] Day -6 for the female study animals.

Appendix G: SERUM CHEMISTRY

List of Serum Chemistry Abbreviations/Units

AST	Aspartate Aminotransferase (U/l)
ALT	Alanine Aminotransferase (U/l)
GGT	Gamma Glutamyl Transferase (U/l)
CK	Creatine Phosphokinase (U/l)
LDH	Lactate Dehydrogenase (U/l)
ALK	Alkaline Phosphatase (U/l)
ALB	Albumin (g/dl)
BILI	Total Bilirubin (mg/dl)
CL	Chloride (Meq/l)
GLU	Glucose (mg/dl)
IRON	Iron (μ g/dl)
MAG	Magnesium (mg/dl)
CAL	Calcium (mg/dl)
PHOS	Phosphorus (mg/dl)
CHOL	Cholesterol (mg/dl)
CR	Creatinine (mg/dl)
TP	Total Protein (g/dl)
URIC	Uric Acid (mg/dl)
NA	Sodium (Meq/l)
K	Potassium (Meq/l)
TRIG	Triglyceride (mg/dl)
BUN	Blood Urea Nitrogen (mg/dl)
A-G	Albumin/Globulin Ratio

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	-13	0.9	34.2	5.7	0.2	5.6	41.	0.9
88A00029	M	4/1	-13	0.7	27.5	6.3	0.2	5.6	46.	1.0
88A00038	F	4/2	-12	0.7	38.4	4.9	0.2	5.0	144.	1.2
88A00041	F	4/2	-12	0.7	26.3	4.3	0.0	4.8	80.	1.5
Parameter means				0.75	31.60	5.30	0.15	5.25	77.8	1.15
Standard deviations				0.10	5.71	0.88	0.10	0.41	47.4	0.26
88A00032	M	1/1	-13	0.7	33.8	6.3	0.2	5.5	40.	0.7
88A00028	M	1/1	-13	0.8	26.5	5.5	0.3	5.3	56.	1.1
88A00043	F	1/2	-12	0.6	26.5	5.7	0.2	5.4	41.	1.0
88A00047	F	1/2	-12	0.8	55.4	4.7	0.4	4.9	76.	1.2
Parameter means				0.73	35.55	5.55	0.28	5.28	53.3	1.00
Standard deviations				0.10	13.67	0.66	0.10	0.26	16.8	0.22
88A00037	M	2/1	-13	0.8	29.4	5.4	0.0	5.1	43.	1.2
88A00035	M	2/1	-13	0.8	35.2	6.4	0.0	5.1	50.	0.9
88A00044	F	2/2	-12	0.7	23.4	5.2	0.2	4.3	60.	1.0
88A00042	F	2/2	-12	0.8	27.1	5.6	0.1	5.6	50.	0.8
Parameter means				0.78	28.78	5.65	0.08	5.03	50.8	0.98
Standard deviations				0.05	4.95	0.53	0.10	0.54	7.0	0.17
88A00033	M	3/1	-13	0.8	30.2	6.2	0.1	5.3	58.	1.0
88A00031	M	3/1	-13	0.5	36.1	6.4	0.1	5.7	38.	0.8
88A00040	F	3/2	-12	0.6	20.1	5.1	0.0	4.9	83.	1.2
88A00046	F	3/2	-12	0.8	41.8	4.4	0.2	4.9	49.	1.0
Parameter means				0.68	32.05	5.53	0.10	5.20	57.0	1.00
Standard deviations				0.15	9.27	0.94	0.08	0.38	19.2	0.16

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89
 Study Number: 88003

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	-13	26.0	15.9	164.92	2.7	0.0	110.	103.9	168.	0.3	61.3	65.9
88A00029	M	4/1	-13	22.4	12.7	141.14	3.1	0.0	106.	66.7	138.	2.3	69.4	104.2
88A00038	F	4/2	-12	41.3	17.9	148.38	2.7	0.0	108.	75.8	187.	0.3	79.9	138.0
88A00041	F	4/2	-12	28.0	21.7	108.31	2.5	0.0	107.	84.7	176.	3.1	87.1	64.1
Parameter means				29.43	17.05	140.69	2.75	0.00	107.8	82.78	167.3	1.50	74.43	93.05
Standard deviations				8.25	3.77	23.77	0.25	0.00	1.7	15.89	21.0	1.42	11.37	35.21
88A00032	M	1/1	-13	28.8	20.7	175.10	2.6	0.0	105.	87.3	137.	2.3	67.6	58.3
88A00028	M	1/1	-13	27.2	13.4	161.26	2.8	0.0	109.	80.8	104.	0.6	88.1	99.7
88A00043	F	1/2	-12	21.4	11.5	126.43	2.8	0.0	109.	81.3	230.	8.2	111.6	84.8
88A00047	F	1/2	-12	39.9	21.0	167.68	2.6	0.0	109.	81.9	110.	4.7	76.6	85.0
Parameter means				29.33	16.65	157.62	2.70	0.00	108.0	82.83	145.3	3.95	85.98	81.95
Standard deviations				7.73	4.91	21.55	0.12	0.00	2.0	3.02	58.3	3.29	19.03	17.24
88A00037	M	2/1	-13	20.9	16.3	150.26	3.0	0.0	109.	112.8	144.	0.4	71.9	40.2
88A00035	M	2/1	-13	28.2	18.3	137.44	2.9	0.0	110.	92.1	100.	1.0	103.9	40.3
88A00044	F	2/2	-12	27.3	11.3	124.52	2.6	0.0	105.	92.3	77.	7.2	96.4	81.4
88A00042	F	2/2	-12	33.1	17.0	121.63	2.5	0.0	111.	81.7	132.	6.1	113.7	59.7
Parameter means				27.38	15.73	133.46	2.75	0.00	108.8	94.73	113.3	3.68	96.48	55.40
Standard deviations				5.01	3.06	13.14	0.24	0.00	2.6	13.03	30.5	3.47	17.85	19.61
88A00033	M	3/1	-13	28.0	19.9	211.86	3.0	0.0	110.	96.6	155.	0.3	77.1	27.8
88A00031	M	3/1	-13	26.1	16.5	154.73	2.8	0.0	113.	77.0	155.	0.7	114.7	74.4
88A00040	F	3/2	-12	25.1	18.5	112.75	2.8	0.0	108.	83.8	244.	6.3	72.1	112.5
88A00046	F	3/2	-12	31.8	15.4	150.44	2.2	0.0	109.	89.1	92.	4.0	84.6	61.5
Parameter means				27.75	17.58	157.45	2.70	0.00	110.0	86.63	161.5	2.83	87.13	69.05
Standard deviations				2.96	2.01	40.89	0.35	0.00	2.2	8.29	62.5	2.85	19.09	35.00

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Study Number: 88003
 Study Start Date: 27-Sep-88

PRINTED: 22-Mar-89
 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	-13	1.45	156.9	10.1	5.5	210.0
88A00029	M	4/1	-13	1.80	157.1	10.8	5.9	198.3
88A00038	F	4/2	-12	2.01	153.7	11.7	6.0	194.4
88A00041	F	4/2	-12	1.75	148.8	10.8	6.2	155.7
Parameter means				1.753	154.13	10.85	5.90	189.60
Standard deviations				0.231	3.88	0.66	0.29	23.55
88A00032	M	1/1	-13	1.53	154.7	10.4	5.7	199.6
88A00028	M	1/1	-13	1.70	156.8	10.8	6.4	272.1
88A00043	F	1/2	-12	1.52	154.1	11.0	7.0	145.0
88A00047	F	1/2	-12	1.71	154.5	11.4	6.4	167.7
Parameter means				1.615	155.03	10.90	6.38	196.10
Standard deviations				0.104	1.21	0.42	0.53	55.40
88A00037	M	2/1	-13	1.51	152.2	10.3	5.8	190.2
88A00035	M	2/1	-13	1.77	157.8	10.2	6.5	239.3
88A00044	F	2/2	-12	1.47	151.7	11.0	7.1	174.8
88A00042	F	2/2	-12	1.71	159.3	11.7	6.9	170.0
Parameter means				1.615	155.25	10.80	6.58	193.58
Standard deviations				0.147	3.86	0.70	0.57	31.68
88A00033	M	3/1	-13	1.75	157.3	10.4	5.3	303.6
88A00031	M	3/1	-13	1.62	155.0	10.1	4.8	200.2
88A00040	F	3/2	-12	1.82	156.3	11.3	7.9	174.6
88A00046	F	3/2	-12	1.54	147.4	11.0	6.2	142.2
Parameter means				1.683	154.00	10.70	6.05	205.15
Standard deviations				0.126	4.50	0.55	1.36	69.79

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	-6	0.6	27.4	5.0	0.3	5.5	31.	0.9
88A00029	M	4/1	-6	0.6	26.0	5.5	0.4	5.1	85	0.9
88A00038	F	4/2	-7	0.5	47.8	5.3	0.1	5.9	102.	2.1
88A00041	F	4/2	-7	0.7	31.2	5.1	0.1	4.5	40.	1.3
Parameter means				0.60	33.10	5.23	0.23	5.25	64.5	1.30
Standard deviations				0.08	10.04	0.22	0.15	0.60	34.4	0.57
88A00032	M	1/1	-6	0.7	35.9	6.0	0.3	4.9	42.	0.7
88A00028	M	1/1	-6	0.7	27.1	5.0	0.4	5.0	49	0.9
88A00043	F	1/2	-7	0.5	28.7	5.7	0.0	5.2	31.	1.4
88A00047	F	1/2	-7	0.7	46.3	5.3	0.0	5.0	38.	1.3
Parameter means				0.65	34.50	5.50	0.18	5.03	40.0	1.08
Standard deviations				0.10	8.75	0.44	0.21	0.13	7.5	0.33
88A00037	M	2/1	-6	0.8	59.3	4.7	0.0	5.4	50.	0.9
88A00035	M	2/1	-6	0.7	28.4	5.3	0.2	5.0	58.	0.9
88A00044	F	2/2	-7	0.6	28.0	5.4	0.0	5.4	53.	1.6
88A00042	F	2/2	-7	0.6	24.9	5.5	0.0	5.0	28.	1.1
Parameter means				0.68	35.15	5.23	0.05	5.20	47.3	1.13
Standard deviations				0.10	16.18	0.36	0.10	0.23	13.3	0.33
88A00033	M	3/1	-6	0.7	27.1	5.2	0.0	4.9	60.	1.0
88A00031	M	3/1	-6	0.5	39.0	5.3	0.3	5.1	35	0.7
88A00040	F	3/2	-7	0.6	24.7	5.7	0.0	5.1	37.	2.1
88A00046	F	3/2	-7	0.6	36.9	5.0	0.0	4.9	26.	1.4
Parameter means				0.60	31.93	5.30	0.08	5.00	39.5	1.30
Standard deviations				0.08	7.08	0.29	0.15	0.12	14.5	0.61

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	-6	31.2	21.1	329.47	2.4	0.0	108.	89.7	157.	4.3	66.2	108.3
88A00029	M	4/1	-6	24.6	17.5	71.33	2.7	0.0	107	63.0	94.	1.2	71.4	98.8
88A00038	F	4/2	-7	53.7	24.1	925.41	3.6	0.0	110.	77.3	245.	NT	89.6	249.0
88A00041	F	4/2	-7	29.9	17.3	132.10	2.9	0.19	108.	88.4	116.	3.9	91.0	70.2
Parameter means				34.85	20.00	364.58	2.90	0.05	108.3	79.60	153.0	3.13	79.55	131.58
Standard deviations				12.89	3.24	389.79	0.51	0.10	1.3	12.39	66.7	1.69	12.61	79.94
88A00032	M	1/1	-6	33.1	24.9	171.89	2.5	0.0	105.	82.2	186.	1.0	82.9	120.9
88A00028	M	1/1	-6	33.3	16.0	156.78	2.3	0.0	110.	98.6	112.	3.3	108.2	90.4
88A00043	F	1/2	-7	22.4	11.2	121.93	3.3	0.0	112.	99.8	227.	6.4	100.8	76.8
88A00047	F	1/2	-7	29.5	16.9	110.67	3.0	0.15	109.	88.3	115.	6.8	73.9	62.2
Parameter means				29.58	17.25	140.32	2.78	0.04	109.0	92.23	160.0	4.38	91.45	87.58
Standard deviations				5.09	5.68	28.78	0.46	0.08	2.9	8.44	56.3	2.74	15.80	25.02
88A00037	M	2/1	-6	32.6	23.8	145.95	2.3	0.0	108.	82.3	126.	5.0	78.0	102.8
88A00035	M	2/1	-6	39.8	22.4	170.35	2.5	0.0	108.	105.1	47.	3.3	117.7	92.2
88A00044	F	2/2	-7	28.9	21.3	121.68	3.3	0.0	110.	102.8	196.	5.7	94.8	65.7
88A00042	F	2/2	-7	28.0	17.5	130.65	2.8	0.0	108.	84.7	230.	4.8	96.8	71.1
Parameter means				32.33	21.25	142.16	2.73	0.00	108.5	93.73	149.8	4.70	96.83	82.95
Standard deviations				5.37	2.70	21.30	0.43	0.00	1.0	11.88	81.0	1.01	16.27	17.49
88A00033	M	3/1	-6	27.5	24.1	137.79	2.6	0.0	110.	106.1	138.	4.1	85.7	62.6
88A00031	M	3/1	-6	35.3	16.6	405.06	2.2	0.0	108.	85.3	167.	3.9	129.1	73.6
88A00040	F	3/2	-7	26.1	14.9	133.19	3.9	0.0	112.	97.2	171.	3.6	70.8	105.9
88A00046	F	3/2	-7	25.3	14.0	118.83	2.9	0.02	113.	96.9	76.	4.8	88.1	70.2
Parameter means				28.55	17.40	198.72	2.90	0.01	110.8	96.38	138.0	4.10	93.43	78.08
Standard deviations				4.59	4.59	137.80	0.73	0.01	2.2	8.53	43.9	0.51	24.98	19.11

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	-6	1.63	151.8	10.2	7.3	183.9
88A00029	M	4/1	-6	1.85	153.1	11.2	6.5	175.2
88A00038	F	4/2	-7	2.30	154.8	10.2	7.9	186.1
88A00041	F	4/2	-7	1.61	153.2	9.7	6.2	150.9
Parameter means				1.848	153.23	10.33	6.98	174.03
Standard deviations				0.321	1.23	0.63	0.77	16.12
88A00032	M	1/1	-6	1.72	153.8	11.3	6.8	200.7
88A00028	M	1/1	-6	1.55	151.6	10.9	6.7	202.5
88A00043	F	1/2	-7	1.63	153.6	9.9	6.1	138.2
88A00047	F	1/2	-7	1.57	153.0	10.1	6.8	146.2
Parameter means				1.618	153.00	10.55	6.60	171.90
Standard deviations				0.076	0.99	0.66	0.34	34.46
88A00037	M	2/1	-6	1.48	150.7	10.9	5.6	197.7
88A00035	M	2/1	-6	1.70	152.8	10.6	7.3	192.1
88A00044	F	2/2	-7	1.71	155.9	10.0	7.4	163.2
88A00042	F	2/2	-7	1.61	154.2	9.8	6.9	145.2
Parameter means				1.625	153.40	10.33	6.80	174.55
Standard deviations				0.107	2.20	0.51	0.83	24.73
88A00033	M	3/1	-6	1.68	153.1	10.7	6.0	249.2
88A00031	M	3/1	-6	1.54	150.7	10.7	7.1	162.2
88A00040	F	3/2	-7	1.82	155.7	9.8	6.7	156.7
88A00046	F	3/2	-7	1.52	151.7	9.7	5.8	135.7
Parameter means				1.640	152.80	10.23	6.40	175.95
Standard deviations				0.140	2.17	0.55	0.61	50.15

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study*	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	0	0.7	29.7	5.1	0.1	5.3	22.	1.2
88A00029	M	4/1	0	0.5	22.8	5.6	0.0	5.7	70.	1.6
88A00038	F	4/2	0	1.0	40.0	5.3	0.8	5.1	46.	2.0
88A00041	F	4/2	0	0.7	29.4	4.8	0.8	5.2	68.	1.0
Parameter means				0.73	30.48	5.20	0.43	5.33	51.5	1.45
Standard deviations				0.21	7.10	0.34	0.43	0.26	22.5	0.44
88A00032	M	1/1	0	0.7	32.2	6.0	0.0	5.2	44.	1.1
88A00028	M	1/1	0	0.6	32.7	5.5	0.3	5.5	68.	1.4
88A00043	F	1/2	0	0.6	29.9	5.3	0.8	5.0	74.	1.2
88A00047	F	1/2	0	0.8	25.0	5.3	0.9	5.1	72.	1.3
Parameter means				0.68	29.95	5.53	0.50	5.20	64.5	1.25
Standard deviations				0.10	3.52	0.33	0.42	0.22	13.9	0.13
88A00037	M	2/1	0	0.6	51.2	5.4	0.0	5.6	46.	1.0
88A00035	M	2/1	0	0.7	33.0	5.3	0.2	5.0	34.	1.4
88A00044	F	2/2	0	0.6	29.0	4.8	0.4	5.0	51.	1.6
88A00042	F	2/2	0	0.7	24.8	5.2	0.8	4.8	43.	1.3
Parameter means				0.65	34.50	5.18	0.35	5.10	43.5	1.33
Standard deviations				0.06	11.63	0.26	0.34	0.35	7.1	0.25
88A00033	M	3/1	0	0.7	29.3	5.5	0.2	4.6	50.	1.5
88A00031	M	3/1	0	0.6	36.1	5.4	0.4	5.1	29.	1.3
88A00040	F	3/2	0	0.7	26.5	5.2	0.8	5.3	53.	1.7
88A00046	F	3/2	0	0.8	30.3	4.7	0.5	5.3	32.	1.1
Parameter means				0.70	30.55	5.20	0.48	5.08	41.0	1.40
Standard deviations				0.08	4.03	0.36	0.25	0.33	12.2	0.26

* Day 0 refers to pretreatment samples taken on the day of dosing.

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
DOG/BEAGLE

Study Number: 88003

Study Start Date: 27-Sep-88

PRINTED: 22-Mar-89

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study*	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	0	34.1	13.1	206.95	2.8	0.17	111.	93.7	71.	4.9	75.0	73.0
88A00029	M	4/1	0	41.2	18.2	329.62	3.4	0.0	110.	91.5	NT	0.0	70.4	420.7
88A00038	F	4/2	0	35.1	24.3	190.41	3.5	0.03	110.	84.1	144.	2.8	76.2	86.5
88A00041	F	4/2	0	35.8	21.4	185.22	2.4	0.11	114.	82.9	115.	0.0	71.1	52.1
Parameter means				36.55	19.25	228.05	3.03	0.08	111.3	88.05	110.0	1.93	73.18	158.08
Standard deviations				3.18	4.80	68.34	0.52	0.08	1.9	5.35	36.8	2.38	2.86	175.65
88A00032	M	1/1	0	30.9	18.2	139.16	3.2	0.02	107.	81.5	124.	1.2	83.2	67.3
88A00028	M	1/1	0	36.4	17.5	161.80	3.2	0.38	110.	77.1	151.	2.9	108.5	119.6
88A00043	F	1/2	0	28.0	16.7	142.95	2.9	0.0	111.	72.5	235.	0.4	93.7	79.0
88A00047	F	1/2	0	32.0	12.7	211.39	2.9	0.11	110.	69.7	97.	2.5	63.8	205.2
Parameter means				31.83	16.28	163.83	3.05	0.13	109.5	75.20	151.8	1.75	87.30	117.78
Standard deviations				3.49	2.46	33.22	0.17	0.18	1.7	5.19	59.7	1.16	18.79	62.44
88A00037	M	2/1	0	34.4	16.3	147.10	2.7	0.0	109.	79.0	NT	0.4	87.6	136.1
88A00035	M	2/1	0	42.9	21.3	197.66	3.2	0.01	112.	85.0	111.	3.8	125.2	107.1
88A00044	F	2/2	0	33.8	14.8	274.45	3.0	0.0	114.	80.7	147.	2.9	98.7	96.8
88A00042	F	2/2	0	36.7	14.2	203.86	2.9	0.08	113.	82.2	101.	3.2	103.4	51.5
Parameter means				36.95	16.65	205.77	2.95	0.02	112.0	81.73	119.7	2.58	103.73	97.88
Standard deviations				4.16	3.22	52.37	0.21	0.04	2.2	2.54	24.2	1.50	15.77	35.11
88A00033	M	3/1	0	33.2	24.2	188.79	3.3	0.0	114.	84.9	145.	1.6	91.7	55.0
88A00031	M	3/1	0	38.5	12.6	229.23	3.1	0.06	112.	89.1	96.	3.7	144.9	90.6
88A00040	F	3/2	0	28.2	18.4	166.54	3.3	0.0	115.	91.7	162.	4.3	70.5	81.0
88A00046	F	3/2	0	26.8	13.8	211.46	2.5	0.08	111.	94.8	74.	2.2	79.0	57.5
Parameter means				31.68	17.25	199.01	3.05	0.04	113.0	90.13	119.3	2.95	96.53	71.03
Standard deviations				5.31	5.26	27.25	0.38	0.04	1.9	4.19	41.1	1.26	33.41	17.53

* Day 0 refers to pretreatment samples taken on the day of dosing.

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study*	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	0	1.56	153.1	10.1	7.0	155.7
88A00029	M	4/1	0	1.72	155.5	9.5	6.6	158.7
88A00038	F	4/2	0	1.84	150.8	10.9	7.1	184.3
88A00041	F	4/2	0	1.72	151.6	11.0	5.8	180.4
Parameter means				1.710	152.75	10.38	6.63	169.78
Standard deviations				0.115	2.07	0.71	0.59	14.66
88A00032	M	1/1	0	1.58	154.7	10.4	6.1	176.1
88A00028	M	1/1	0	1.87	155.9	10.4	7.9	216.6
88A00043	F	1/2	0	1.73	147.6	10.1	5.6	141.7
88A00047	F	1/2	0	1.64	148.5	10.6	6.5	156.7
Parameter means				1.705	151.68	10.38	6.53	172.78
Standard deviations				0.126	4.23	0.21	0.99	32.43
88A00037	M	2/1	0	1.65	154.8	10.1	5.5	192.6
88A00035	M	2/1	0	1.97	155.8	9.9	7.4	169.4
88A00044	F	2/2	0	1.55	150.5	10.8	6.0	159.4
88A00042	F	2/2	0	1.59	148.0	10.8	6.3	154.6
Parameter means				1.690	152.28	10.40	6.30	169.00
Standard deviations				0.191	3.66	0.47	0.80	16.90
88A00033	M	3/1	0	1.90	155.8	10.4	6.3	244.1
88A00031	M	3/1	0	1.52	152.2	10.2	6.7	152.5
88A00040	F	3/2	0	1.69	151.5	10.4	6.4	143.8
88A00046	F	3/2	0	1.55	147.1	10.7	6.1	138.0
Parameter means				1.665	151.65	10.43	6.38	169.60
Standard deviations				0.173	3.57	0.21	0.25	50.02

* Day 0 refers to pretreatment samples taken on the day of dosing.

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	0/6hr	0.7	30.6	5.0	0.1	5.4	24.	1.1
88A00029	M	4/1	0/6hr	0.7	21.7	5.5	0.1	5.6	74.	1.5
88A00038	F	4/2	0/6hr	0.8	39.2	5.1	0.8	4.9	81.	2.1
88A00041	F	4/2	0/6hr	0.5	36.6	4.8	0.8	4.6	50.	1.3
Parameter means				0.68	32.03	5.10	0.45	5.13	57.3	1.50
Standard deviations				0.13	7.77	0.29	0.40	0.46	25.8	0.43
88A00032	M	1/1	0/6hr	0.6	434.1	5.4	0.0	4.1	16.	0.8
88A00028	M	1/1	0/6hr	0.5	83.7	4.6	0.0	4.4	45.	1.4
88A00043	F	1/2	0/6hr	0.5	316.7	4.6	0.9	3.8	79.	1.3
88A00047	F	1/2	0/6hr	0.6	111.7	4.5	0.9	4.0	17.	1.0
Parameter means				0.55	236.55	4.78	0.45	4.08	39.3	1.13
Standard deviations				0.06	167.73	0.42	0.52	0.25	29.7	0.28
88A00037	M	2/1	0/6hr	0.5	250.9	4.9	0.2	4.7	66.	1.5
88A00035	M	2/1	0/6hr	0.5	74.7	5.6	0.1	4.4	50.	1.2
88A00044	F	2/2	0/6hr	0.5	273.9	5.0	0.9	4.1	74.	2.3
88A00042	F	2/2	0/6hr	0.5	111.7	5.4	0.8	4.4	38.	1.4
Parameter means				0.50	177.80	5.23	0.50	4.40	57.0	1.60
Standard deviations				0.00	99.29	0.33	0.41	0.24	16.1	0.48
88A00033	M	3/1	0/6hr	0.6	26.0	4.8	0.1	5.2	35.	1.3
88A00031	M	3/1	0/6hr	0.7	29.9	4.6	0.2	5.0	24.	1.2
88A00040	F	3/2	0/6hr	0.7	29.7	4.4	0.9	4.9	42.	1.9
88A00046	F	3/2	0/6hr	0.6	27.1	4.0	0.8	4.8	42.	1.3
Parameter means				0.65	28.18	4.45	0.50	4.98	35.8	1.43
Standard deviations				0.06	1.93	0.34	0.41	0.17	8.5	0.32

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	0/6hr	34.0	17.0	193.10	2.7	0.15	113.	95.8	101.	9.1	66.6	73.9
88A00029	M	4/1	0/6hr	21.4	18.6	82.44	3.3	0.0	114.	82.9	312.	1.0	61.5	52.8
88A00038	F	4/2	0/6hr	34.5	24.4	180.50	3.4	0.0	119.	87.5	246.	1.8	76.4	58.7
88A00041	F	4/2	0/6hr	38.9	20.2	195.77	2.7	0.09	115.	85.0	110.	0.6	74.2	42.7
Parameter means				32.20	20.05	162.95	3.03	0.06	115.3	87.80	192.3	3.13	69.68	57.03
Standard deviations				7.53	3.18	54.09	0.38	0.07	2.6	5.66	103.8	4.01	6.88	13.05
88A00032	M	1/1	0/6hr	254.5	15.7	326.59	2.4	0.02	112.	83.8	117.	3.2	165.9	122.0
88A00028	M	1/1	0/6hr	91.3	16.8	196.49	2.7	0.25	116.	77.7	24.	2.2	181.4	126.0
88A00043	F	1/2	0/6hr	162.6	7.1	147.21	2.6	0.0	118.	83.0	35.	3.5	164.1	73.6
88A00047	F	1/2	0/6hr	111.3	10.2	470.60	2.3	0.03	116.	79.4	92.	2.6	127.6	376.8
Parameter means				154.93	12.45	285.22	2.50	0.08	115.5	80.98	67.0	2.88	159.75	174.60
Standard deviations				72.86	4.59	144.91	0.18	0.12	2.5	2.90	44.7	0.59	22.80	136.89
88A00037	M	2/1	0/6hr	74.7	14.8	155.60	3.0	0.0	116.	86.2	152.	7.0	72.6	97.3
88A00035	M	2/1	0/6hr	59.4	13.6	283.25	3.1	0.0	115.	80.6	149.	7.9	107.1	72.8
88A00044	F	2/2	0/6hr	176.8	14.7	504.36	3.5	0.0	117.	94.7	196.	1.9	98.8	98.6
88A00042	F	2/2	0/6hr	73.7	16.8	269.10	3.1	0.0	115.	69.7	89.	1.1	101.6	65.9
Parameter means				96.15	14.98	303.08	3.18	0.00	115.8	82.80	146.5	4.48	95.03	83.65
Standard deviations				54.22	1.33	145.84	0.22	0.00	1.0	10.48	43.9	3.47	15.34	16.76
88A00033	M	3/1	0/6hr	42.0	22.3	98.83	2.7	0.0	113.	104.4	127.	5.6	155.7	45.9
88A00031	M	3/1	0/6hr	53.9	17.4	274.92	2.5	0.01	116.	99.8	87.	2.3	220.7	56.5
88A00040	F	3/2	0/6hr	48.3	17.1	123.94	2.8	0.0	116.	75.9	124.	4.6	144.0	56.1
88A00046	F	3/2	0/6hr	40.0	23.3	102.71	2.2	0.0	112.	80.2	84.	0.0	150.2	51.3
Parameter means				46.05	20.03	150.10	2.55	0.00	114.3	90.08	105.5	3.13	167.65	52.45
Standard deviations				6.32	3.23	83.94	0.26	0.01	2.1	14.12	23.2	2.50	35.69	4.96

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS J
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	0/6hr	1.53	152.7	9.1	7.5	162.2
88A00029	M	4/1	0/6hr	1.82	155.6	10.6	7.3	160.2
88A00038	F	4/2	0/6hr	1.94	146.1	11.4	8.3	191.5
88A00041	F	4/2	0/6hr	1.68	152.2	10.5	6.3	183.4
Parameter means				1.743	151.65	10.40	7.35	174.33
Standard deviations				0.177	3.99	0.96	0.82	15.53
88A00032	M	1/1	0/6hr	1.30	155.8	9.1	6.8	135.5
88A00028	M	1/1	0/6hr	1.51	158.0	8.9	6.8	170.0
88A00043	F	1/2	0/6hr	1.19	154.3	9.4	5.7	122.6
88A00047	F	1/2	0/6hr	1.27	158.1	9.7	7.5	119.6
Parameter means				1.318	156.55	9.28	6.70	136.93
Standard deviations				0.136	1.84	0.35	0.74	23.10
88A00037	M	2/1	0/6hr	1.48	157.0	9.9	5.9	184.7
88A00035	M	2/1	0/6hr	1.60	156.0	10.0	7.8	165.5
88A00044	F	2/2	0/6hr	1.48	154.8	10.8	5.9	177.4
88A00042	F	2/2	0/6hr	1.33	155.1	10.3	6.4	171.6
Parameter means				1.473	155.73	10.25	6.50	174.80
Standard deviations				0.111	0.99	0.40	0.90	8.20
88A00033	M	3/1	0/6hr	1.67	154.6	9.6	7.7	180.0
88A00031	M	3/1	0/6hr	1.37	152.2	9.3	6.6	115.7
88A00040	F	3/2	0/6hr	1.40	152.2	9.8	6.4	117.6
88A00046	F	3/2	0/6hr	1.53	146.4	9.9	7.4	111.4
Parameter means				1.493	151.35	9.65	7.03	131.18
Standard deviations				0.137	3.49	0.26	0.62	32.65

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
DOG/BEAGLE

Expanded Statistical Table for COBAS I
Study Number: 88003

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	1/24hr	0.7	29.6	5.1	0.3	4.6	20.	1.2
88A00029	M	4/1	1/24hr	0.7	21.3	6.1	0.2	5.2	54.	1.3
88A00038	F	4/2	1/24hr	0.8	39.1	5.2	0.9	4.7	56.	1.6
88A00041	F	4/2	1/24hr	0.7	35.6	4.8	0.8	4.5	51.	1.4
Parameter means				0.73	31.40	5.30	0.55	4.75	45.3	1.38
Standard deviations				0.05	7.79	0.56	0.35	0.31	17.0	0.17
88A00032	M	1/1	1/24hr	0.8	326.5	5.7	0.2	4.3	19.	1.1
88A00028	M	1/1	1/24hr	0.6	67.1	4.9	0.0	5.2	22.	1.4
88A00043	F	1/2	1/24hr	0.7	229.0	5.0	0.9	4.4	38.	1.3
88A00047	F	1/2	1/24hr	0.9	84.0	4.7	0.9	4.9	48.	1.2
Parameter means				0.75	176.65	5.08	0.50	4.70	31.8	1.25
Standard deviations				0.13	123.53	0.43	0.47	0.42	13.7	0.13
88A00037	M	2/1	1/24hr	0.7	175.3	5.0	0.0	4.8	54.	1.4
88A00035	M	2/1	1/24hr	0.8	61.5	5.5	0.0	4.5	33.	1.3
88A00044	F	2/2	1/24hr	0.8	170.3	4.9	0.8	4.5	66.	1.8
88A00042	F	2/2	1/24hr	0.7	73.9	5.0	0.8	4.7	37.	1.2
Parameter means				0.75	120.25	5.10	0.40	4.63	47.5	1.43
Standard deviations				0.06	60.92	0.27	0.46	0.15	15.3	0.26
88A00033	M	3/1	1/24hr	0.8	27.2	5.1	0.1	4.4	41.	1.7
88A00031	M	3/1	1/24hr	0.7	32.4	4.9	0.3	5.0	20.	1.1
88A00040	F	3/2	1/24hr	0.8	30.9	4.9	0.9	5.1	35.	1.6
88A00046	F	3/2	1/24hr	0.9	31.0	4.2	0.8	4.9	32.	1.7
Parameter means				0.80	30.38	4.78	0.53	4.85	32.0	1.53
Standard deviations				0.08	2.22	0.39	0.39	0.31	8.8	0.29

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	1/24hr	29.6	12.1	161.60	2.8	0.14	113.	87.1	40.	3.6	68.2	105.7
88A00029	M	4/1	1/24hr	21.9	16.6	122.95	3.5	0.00	114.	85.3	162.	2.1	69.1	126.4
88A00038	F	4/2	1/24hr	44.9	19.6	461.40	3.2	0.0	110.	68.1	121.	0.0	73.4	318.6
88A00041	F	4/2	1/24hr	36.4	14.9	199.19	2.8	0.10	108.	62.0	77.	1.8	76.2	153.5
Parameter means				33.20	15.80	236.29	3.08	0.06	111.3	75.63	100.0	1.88	71.73	176.05
Standard deviations				9.79	3.14	153.27	0.34	0.07	2.8	12.48	53.0	1.48	3.75	97.03
88A00032	M	1/1	1/24hr	186.0	13.0	205.57	2.9	0.07	109.	88.7	72.	3.7	310.7	54.3
88A00028	M	1/1	1/24hr	108.9	17.0	278.43	2.8	0.34	114.	75.1	55.	4.8	333.4	133.7
88A00043	F	1/2	1/24hr	115.5	9.2	121.95	2.8	0.04	110.	77.1	71.	5.0	303.9	65.2
88A00047	F	1/2	1/24hr	96.7	12.4	193.10	2.6	0.12	113.	72.8	27.	4.2	242.1	145.7
Parameter means				126.78	12.90	199.76	2.78	0.14	111.5	78.43	56.3	4.43	297.53	99.73
Standard deviations				40.24	3.20	64.09	0.13	0.14	2.4	7.07	21.0	0.59	39.04	46.63
88A00037	M	2/1	1/24hr	32.0	17.1	142.57	2.9	0.0	112.	104.2	131.	1.9	75.9	69.9
88A00035	M	2/1	1/24hr	37.5	14.7	158.88	3.1	0.05	109.	106.9	65.	2.5	111.2	66.9
88A00044	F	2/2	1/24hr	39.5	13.0	174.36	3.2	0.07	112.	73.0	82.	3.4	104.5	125.9
88A00042	F	2/2	1/24hr	36.7	11.7	139.02	2.7	0.02	112.	72.1	113.	2.3	101.2	61.3
Parameter means				36.43	14.13	153.71	2.98	0.04	111.3	89.05	97.8	2.53	98.20	81.00
Standard deviations				3.18	2.33	16.26	0.22	0.03	1.5	19.09	29.8	0.63	15.44	30.14
88A00033	M	3/1	1/24hr	74.5	15.9	133.98	3.2	0.02	113.	114.2	36.	3.2	312.4	52.0
88A00031	M	3/1	1/24hr	85.3	18.6	187.11	2.5	0.0	115.	87.4	193.	2.9	409.0	61.0
88A00040	F	3/2	1/24hr	79.6	13.3	105.57	3.0	0.00	113.	80.5	66.	4.4	270.6	81.8
88A00046	F	3/2	1/24hr	79.3	13.4	275.51	2.6	0.0	111.	90.9	37.	1.8	302.2	97.2
Parameter means				79.68	15.30	175.54	2.83	0.01	113.0	93.25	83.0	3.08	323.55	73.00
Standard deviations				4.42	2.51	74.72	0.33	0.01	1.6	14.62	74.6	1.07	59.68	20.40

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Study Start Date: 27-Sep-88
 ACUTE/ACUTE INTRAVENOUS

PRINTED: 22-Mar-89
 Study Number: 88003

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	1/24hr	1.44	152.9	9.1	6.1	158.2
88A00029	M	4/1	1/24hr	1.78	157.0	10.4	6.6	168.1
88A00038	F	4/2	1/24hr	1.80	150.6	10.9	6.1	188.5
88A00041	F	4/2	1/24hr	1.56	148.1	10.4	6.2	185.2
Parameter means				1.645	152.15	10.20	6.25	175.00
Standard deviations				0.175	3.78	0.77	0.24	14.33
88A00032	M	1/1	1/24hr	1.22	153.2	9.8	5.7	152.0
88A00028	M	1/1	1/24hr	1.57	152.0	9.4	7.1	179.8
88A00043	F	1/2	1/24hr	1.37	149.7	10.4	5.7	133.1
88A00047	F	1/2	1/24hr	1.56	150.3	10.3	7.0	147.9
Parameter means				1.430	151.30	9.98	6.38	153.20
Standard deviations				0.168	1.60	0.46	0.78	19.50
88A00037	M	2/1	1/24hr	1.45	153.2	10.2	5.3	197.1
88A00035	M	2/1	1/24hr	1.51	154.7	9.9	6.6	168.2
88A00044	F	2/2	1/24hr	1.51	149.4	10.4	5.2	171.7
88A00042	F	2/2	1/24hr	1.54	146.9	10.4	5.9	157.2
Parameter means				1.503	151.05	10.23	5.75	173.55
Standard deviations				0.038	3.55	0.24	0.65	16.87
88A00033	M	3/1	1/24hr	1.61	153.6	9.8	5.9	202.2
88A00031	M	3/1	1/24hr	1.39	153.4	9.6	7.8	137.0
88A00040	F	3/2	1/24hr	1.80	153.3	10.9	6.1	142.0
88A00046	F	3/2	1/24hr	1.54	148.3	10.7	6.1	128.7
Parameter means				1.585	152.15	10.25	6.48	152.48
Standard deviations				0.170	2.57	0.65	0.89	33.60

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	2/48hr	0.7	29.7	4.7	0.2	4.9	41.	1.6
88A00029	M	4/1	2/48hr	0.6	19.5	6.0	0.1	4.8	41.	1.2
88A00038	F	4/2	2/48hr	0.9	38.7	5.6	0.2	4.8	49.	1.9
88A00041	F	4/2	2/48hr	0.6	35.3	5.2	0.0	5.2	68.	2.5
Parameter means				0.70	30.80	5.38	0.13	4.93	49.8	1.80
Standard deviations				0.14	8.40	0.56	0.10	0.19	12.7	0.55
88A00032	M	1/1	2/48hr	0.8	251.1	5.5	0.3	4.6	33.	1.0
88A00028	M	1/1	2/48hr	0.7	58.5	5.0	0.3	5.0	59.	1.4
88A00043	F	1/2	2/48hr	0.6	181.0	5.5	0.2	4.9	32.	1.5
88A00047	F	1/2	2/48hr	0.7	72.0	5.1	0.1	5.1	48.	1.9
Parameter means				0.70	140.65	5.28	0.23	4.90	43.0	1.45
Standard deviations				0.08	91.81	0.26	0.10	0.22	12.9	0.37
88A00037	M	2/1	2/48hr	0.7	126.7	4.6	0.1	5.5	66.	2.3
88A00035	M	2/1	2/48hr	0.8	50.8	5.0	0.1	4.9	34.	1.6
88A00044	F	2/2	2/48hr	0.7	116.1	4.9	0.1	4.2	42.	1.9
88A00042	F	2/2	2/48hr	0.8	60.0	5.6	0.1	5.1	37.	1.5
Parameter means				0.75	88.40	5.03	0.10	4.93	44.8	1.83
Standard deviations				0.06	38.53	0.42	0.00	0.54	14.5	0.36
88A00033	M	3/1	2/48hr	0.7	28.4	4.6	0.1	4.8	42.	1.8
88A00031	M	3/1	2/48hr	0.6	34.1	4.8	0.3	4.9	23.	1.3
88A00040	F	3/2	2/48hr	0.7	34.0	5.0	0.1	5.3	50.	1.5
88A00046	F	3/2	2/48hr	0.8	32.4	4.6	0.1	4.5	28.	2.0
Parameter means				0.70	32.23	4.75	0.15	4.88	35.8	1.65
Standard deviations				0.08	2.67	0.19	0.10	0.33	12.4	0.31

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	2/48hr	29.4	15.9	194.11	2.9	0.09	114.	86.3	98.	6.1	73.9	141.3
88A00029	M	4/1	2/48hr	24.9	15.8	162.73	3.3	0.05	108.	75.8	173.	3.0	72.9	218.9
88A00038	F	4/2	2/48hr	37.1	16.0	211.29	3.6	0.0	112.	99.0	104.	0.0	73.4	121.7
88A00041	F	4/2	2/48hr	89.9	19.4	95.77	3.7	0.0	115.	90.4	112.	3.5	334.7	82.2
Parameter means				45.33	16.78	165.98	3.38	0.04	112.3	87.88	121.8	3.15	138.73	141.03
Standard deviations				30.14	1.75	50.94	0.36	0.04	3.1	9.63	34.6	2.50	130.65	57.44
88A00032	M	1/1	2/48hr	127.9	23.0	180.14	2.8	0.01	106.	107.7	97.	7.9	374.5	77.3
88A00028	M	1/1	2/48hr	107.5	16.7	142.76	2.9	0.31	111.	77.2	138.	4.5	403.9	120.3
88A00043	F	1/2	2/48hr	86.4	11.4	127.61	3.3	0.0	112.	82.0	91.	5.9	376.2	76.8
88A00047	F	1/2	2/48hr	103.2	14.6	404.81	3.4	0.0	112.	84.7	138.	2.3	299.5	424.0
Parameter means				106.25	16.43	213.83	3.10	0.08	110.3	87.90	116.0	5.15	363.53	174.60
Standard deviations				17.06	4.90	129.22	0.29	0.15	2.9	13.56	25.5	2.36	44.76	167.51
88A00037	M	2/1	2/48hr	25.0	20.6	120.44	3.2	0.0	112.	95.3	169.	6.4	77.7	84.7
88A00035	M	2/1	2/48hr	33.0	20.3	150.15	3.1	0.04	109.	97.7	65.	6.8	107.9	65.8
88A00044	F	2/2	2/48hr	29.2	13.2	139.72	3.2	0.00	110.	89.6	88.	2.7	88.9	77.2
88A00042	F	2/2	2/48hr	33.8	15.1	147.30	3.3	0.02	116.	93.8	115.	4.1	98.5	55.3
Parameter means				30.25	17.30	139.40	3.20	0.02	111.8	94.10	109.3	5.00	93.25	70.75
Standard deviations				4.03	3.72	13.39	0.08	0.02	3.1	3.40	44.8	1.94	12.95	12.90
88A00033	M	3/1	2/48hr	89.1	23.0	173.78	3.0	0.0	112.	109.3	92.	8.0	402.3	50.2
88A00031	M	3/1	2/48hr	105.8	18.0	876.52	2.7	0.06	109.	87.2	66.	4.5	515.6	115.7
88A00040	F	3/2	2/48hr	35.5	25.9	194.06	3.0	0.0	113.	86.4	157.	0.7	77.6	175.2
88A00046	F	3/2	2/48hr	84.8	14.4	119.92	3.1	0.00	110.	84.7	73.	2.9	364.5	46.6
Parameter means				78.80	20.33	341.07	2.95	0.02	111.0	91.90	97.0	4.03	340.00	96.93
Standard deviations				30.25	5.12	358.33	0.17	0.03	1.8	11.65	41.5	3.07	186.34	61.09

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I PRINTED: 22-Mar-89
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129 Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS
 DOG/BEAGLE

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	2/48hr	1.65	154.8	9.9	7.4	166.7
88A00029	M	4/1	2/48hr	1.67	155.5	10.0	7.3	166.3
88A00038	F	4/2	2/48hr	1.67	152.6	10.8	5.8	179.9
88A00041	F	4/2	2/48hr	1.80	151.1	10.7	6.7	141.9
Parameter means				1.698	153.50	10.35	6.80	163.70
Standard deviations				0.069	2.02	0.47	0.73	15.85
88A00032	M	1/1	2/48hr	1.68	152.8	10.3	6.5	150.9
88A00028	M	1/1	2/48hr	1.63	154.4	9.7	7.7	213.6
88A00043	F	1/2	2/48hr	1.49	149.4	10.6	6.4	131.5
88A00047	F	1/2	2/48hr	1.87	151.6	11.0	7.9	148.8
Parameter means				1.668	152.05	10.40	7.13	161.20
Standard deviations				0.157	2.11	0.55	0.78	36.00
88A00037	M	2/1	2/48hr	1.73	152.3	10.3	6.7	197.2
88A00035	M	2/1	2/48hr	1.73	153.2	10.0	7.4	159.5
88A00044	F	2/2	2/48hr	1.52	141.1	9.6	5.8	150.4
88A00042	F	2/2	2/48hr	1.64	151.9	10.7	7.0	165.3
Parameter means				1.655	149.63	10.15	6.73	168.10
Standard deviations				0.099	5.71	0.47	0.68	20.35
88A00033	M	3/1	2/48hr	1.43	153.2	10.2	7.2	218.0
88A00031	M	3/1	2/48hr	1.43	151.0	9.6	7.2	135.4
88A00040	F	3/2	2/48hr	1.85	152.0	10.4	8.2	179.0
88A00046	F	3/2	2/48hr	1.45	144.2	10.4	5.5	121.2
Parameter means				1.540	150.10	10.15	7.03	163.40
Standard deviations				0.207	4.03	0.38	1.12	43.93

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	3/72hr	0.7	29.6	4.7	0.8	5.0	34.	1.4
88A00029	M	4/1	3/72hr	0.6	21.7	5.8	0.8	4.9	52.	1.5
88A00038	F	4/2	3/72hr	0.9	38.5	5.4	0.1	4.8	48.	1.9
88A00041	F	4/2	3/72hr	0.8	35.3	5.6	0.2	5.6	76.	1.5
Parameter means				0.75	31.28	5.38	0.48	5.08	52.5	1.58
Standard deviations				0.13	7.37	0.48	0.38	0.36	17.5	0.22
88A00032	M	1/1	3/72hr	0.8	219.7	5.8	0.9	4.8	44.	1.1
88A00028	M	1/1	3/72hr	0.6	55.5	5.2	0.9	5.1	62.	1.1
88A00043	F	1/2	3/72hr	0.5	142.1	5.4	0.2	4.7	80.	1.4
88A00047	F	1/2	3/72hr	0.8	65.3	5.7	0.1	5.5	54.	1.8
Parameter means				0.68	120.65	5.53	0.53	5.03	60.0	1.35
Standard deviations				0.15	76.55	0.28	0.43	0.36	15.2	0.33
88A00037	M	2/1	3/72hr	0.7	102.3	4.9	0.8	5.0	61.	1.5
88A00035	M	2/1	3/72hr	0.8	45.6	5.2	0.8	4.4	40.	1.6
88A00044	F	2/2	3/72hr	0.7	95.6	5.3	0.1	4.8	47.	2.5
88A00042	F	2/2	3/72hr	0.7	49.6	5.6	0.1	5.0	37.	1.4
Parameter means				0.73	73.28	5.25	0.45	4.80	46.3	1.75
Standard deviations				0.05	29.82	0.29	0.40	0.28	10.7	0.51
88A00033	M	3/1	3/72hr	0.8	33.8	5.2	0.9	4.5	47.	1.3
88A00031	M	3/1	3/72hr	0.7	37.5	5.0	0.5	5.2	31.	1.1
88A00040	F	3/2	3/72hr	0.6	32.1	5.1	0.2	14.1*	57.	2.8
88A00046	F	3/2	3/72hr	0.8	36.0	5.1	0.1	4.8	37.	2.2
Parameter means				0.73	34.85	5.10	0.43	4.83	43.0	1.85
Standard deviations				0.10	2.38	0.08	0.36	0.35	11.4	0.79

* Value considered spurious not included in mean or standard deviation.

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	3/72hr	28.8	21.8	140.57	2.8	0.0	117.	90.5	162.	1.6	62.5	89.8
88A00029	M	4/1	3/72hr	24.0	13.4	143.29	3.5	0.0	115.	79.0	205.	1.5	68.6	130.8
88A00038	F	4/2	3/72hr	36.0	16.2	218.38	3.5	0.02	114.	82.6	95.	1.0	64.4	107.2
88A00041	F	4/2	3/72hr	32.0	23.5	132.48	3.4	0.0	120.	86.3	201.	0.0	64.0	98.7
Parameter means				30.20	18.73	158.68	3.30	0.01	116.5	84.60	165.8	1.03	64.88	106.63
Standard deviations				5.08	4.73	40.06	0.34	0.01	2.6	4.93	51.0	0.73	2.61	17.61
88A00032	M	1/1	3/72hr	95.4	16.0	129.69	3.0	0.0	111.	100.4	100.	0.0	359.0	56.8
88A00028	M	1/1	3/72hr	91.1	15.2	183.85	2.7	0.26	114.	70.7	84.	4.0	362.8	124.9
88A00043	F	1/2	3/72hr	63.3	12.9	102.81	3.2	0.0	109.	80.0	126.	2.9	345.3	63.7
88A00047	F	1/2	3/72hr	78.1	15.2	168.18	3.6	0.02	118.	84.1	167.	3.4	326.8	137.3
Parameter means				81.98	14.83	146.13	3.13	0.07	113.0	83.80	119.3	2.58	348.48	95.68
Standard deviations				14.46	1.34	36.77	0.38	0.13	3.9	12.41	36.2	1.77	16.29	41.31
88A00037	M	2/1	3/72hr	25.4	17.6	107.81	2.9	0.0	114.	78.7	133.	0.0	72.3	91.9
88A00035	M	2/1	3/72hr	34.3	17.9	179.23	3.2	0.0	113.	107.2	55.	2.4	104.9	64.8
88A00044	F	2/2	3/72hr	31.5	13.1	152.13	3.8	0.0	116.	96.2	152.	2.7	92.5	63.9
88A00042	F	2/2	3/72hr	33.9	17.3	132.56	3.2	0.0	115.	75.0	187.	0.0	88.2	81.1
Parameter means				31.28	16.48	142.93	3.28	0.00	114.5	89.28	131.8	1.28	89.48	75.43
Standard deviations				4.11	2.26	30.24	0.38	0.00	1.3	15.11	55.8	1.48	13.46	13.53
88A00033	M	3/1	3/72hr	91.4	18.7	197.45	3.0	0.0	114.	112.9	87.	1.8	398.9	81.8
88A00031	M	3/1	3/72hr	86.3	18.9	189.61	2.7	0.0	113.	74.8	154.	3.3	515.7	81.4
88A00040	F	3/2	3/72hr	74.4	16.6	107.79	3.7	0.0	113.	85.1	15.	0.0	222.4	101.1
88A00046	F	3/2	3/72hr	85.7	14.4	207.10	3.5	0.0	112.	87.5	70.	2.8	388.4	77.0
Parameter means				84.45	17.15	175.49	3.23	0.00	113.0	90.08	81.5	1.98	381.35	85.33
Standard deviations				7.17	2.11	45.69	0.46	0.00	0.8	16.18	57.3	1.46	120.65	10.74

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	3/72hr	1.58	149.5	9.5	6.9	169.4
88A00029	M	4/1	3/72hr	1.77	155.1	11.0	6.8	174.1
88A00038	F	4/2	3/72hr	1.76	155.3	11.1	5.8	170.7
88AC0041	F	4/2	3/72hr	1.86	160.1	11.3	7.0	188.4
Parameter means				1.743	155.00	10.73	6.63	175.65
Standard deviations				0.117	4.33	0.83	0.56	8.73
88A00032	M	1/1	3/72hr	1.56	150.9	10.9	6.5	170.8
88A00028	M	1/1	3/72hr	1.61	152.9	10.5	8.0	240.8
88A00043	F	1/2	3/72hr	1.53	145.0	10.4	6.2	134.7
88A00047	F	1/2	3/72hr	1.64	161.1	11.7	7.5	155.4
Parameter means				1.585	152.48	10.88	7.05	175.43
Standard deviations				0.049	6.66	0.59	0.84	46.02
88A00037	M	2/1	3/72hr	1.57	150.0	11.0	7.2	202.7
88A00035	M	2/1	3/72hr	1.59	148.8	10.1	7.1	164.6
88A00044	F	2/2	3/72hr	1.46	152.9	11.2	6.6	156.3
88A00042	F	2/2	3/72hr	1.60	152.7	10.6	7.2	162.7
Parameter means				1.555	151.10	10.73	7.03	171.58
Standard deviations				0.065	2.02	0.49	0.29	21.05
88A00033	M	3/1	3/72hr	1.72	153.6	10.7	6.2	233.8
88A00031	M	3/1	3/72hr	1.53	149.7	10.5	6.5	153.0
88A00040	F	3/2	3/72hr	0.25	150.7	NT	6.3	145.2
88A00046	F	3/2	3/72hr	1.47	151.3	11.3	6.1	139.1
Parameter means				1.243	151.33	10.83	6.28	167.78
Standard deviations				0.670	1.65	0.42	0.17	44.38

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	7	0.7	26.4	4.1	0.8	4.6	36.	1.2
88A00029	M	4/1	7	0.6	23.0	5.5	0.9	5.2	53.	1.1
88A00038	F	4/2	7	0.9	36.7	5.4	0.2	4.6	75.	2.6
88A00041	F	4/2	7	0.8	32.1	5.4	0.2	5.0	62.	1.8
Parameter means				0.75	29.55	5.10	0.53	4.85	56.5	1.68
Standard deviations				0.13	6.07	0.67	0.38	0.30	16.4	0.69
88A00032	M	1/1	7	0.7	87.2	5.6	0.6	5.3	45.	1.0
88A00028	M	1/1	7	0.6	40.8	5.0	1.0	5.6	75.	1.2
88A00043	F	1/2	7	0.6	62.8	5.7	0.2	4.9	43.	1.6
88A00047	F	1/2	7	0.8	37.7	5.2	0.1	5.2	52.	1.7
Parameter means				0.68	57.13	5.38	0.48	5.25	53.8	1.38
Standard deviations				0.10	22.95	0.33	0.41	0.29	14.7	0.33
88A00037	M	2/1	7	0.7	49.0	5.2	0.8	4.8	55.	1.2
88A00035	M	2/1	7	0.5	32.0	3.9	0.8	3.9	72.	1.3
88A00044	F	2/2	7	0.6	42.0	4.4	0.1	4.0	51.	3.0
88A00042	F	2/2	7	0.6	29.3	5.1	0.0	4.6	38.	2.0
Parameter means				0.60	38.08	4.65	0.43	4.33	54.0	1.88
Standard deviations				0.08	9.10	0.61	0.43	0.44	14.0	0.83
88A00033	M	3/1	7	0.7	27.6	5.1	0.9	5.1	70.	1.2
88A00031	M	3/1	7	0.7	33.8	5.1	0.9	4.9	34.	1.2
88A00040	F	3/2	7	0.8	22.9	5.1	0.2	4.8	32.	2.8
88A00046	F	3/2	7	0.7	31.6	5.0	0.0	4.8	33.	2.4
Parameter means				0.73	28.98	5.08	0.50	4.90	42.3	1.90
Standard deviations				0.05	4.79	0.05	0.47	0.14	18.5	0.82

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	7	26.5	13.5	163.72	2.3	0.06	107.	77.3	65.	4.8	55.9	64.3
88A00029	M	4/1	7	29.2	17.1	144.89	2.9	0.0	115.	79.6	186.	0.0	62.8	130.2
88A00038	F	4/2	7	42.4	18.8	261.95	3.9	0.05	116.	88.3	89.	0.9	67.9	186.3
88A00041	F	4/2	7	39.0	24.0	262.68	3.5	0.28	117.	75.6	118.	1.4	76.0	112.4
Parameter means				34.28	18.35	208.31	3.15	0.10	113.8	80.20	114.5	1.78	65.65	123.30
Standard deviations				7.63	4.37	62.83	0.70	0.12	4.6	5.64	52.4	2.10	8.47	50.39
88A00032	M	1/1	7	29.8	27.0	170.32	2.8	0.01	112.	86.0	82.	2.1	83.6	44.1
88A00028	M	1/1	7	39.9	14.9	408.81	2.8	0.34	112.	74.6	149.	1.8	101.9	112.5
88A00043	F	1/2	7	27.5	11.5	157.54	3.5	0.08	114.	80.0	106.	3.7	100.9	110.6
88A00047	F	1/2	7	30.8	16.2	216.32	3.3	0.17	111.	79.1	158.	2.5	68.9	192.5
Parameter means				32.00	17.40	238.25	3.10	0.15	112.3	79.93	123.8	2.53	88.83	114.93
Standard deviations				5.44	6.70	116.48	0.36	0.14	1.3	4.69	35.9	0.83	15.72	60.71
88A00037	M	2/1	7	30.1	20.9	332.81	2.8	0.0	110.	93.9	87.	4.3	73.5	105.0
88A00035	M	2/1	7	37.1	17.4	150.00	2.2	0.0	100.	70.7	28.	3.3	86.6	38.6
88A00044	F	2/2	7	31.6	15.6	174.44	3.3	0.02	106.	88.3	91.	2.9	87.4	88.5
88A00042	F	2/2	7	32.6	17.2	133.39	3.4	0.07	113.	82.4	266.	2.5	90.3	79.0
Parameter means				32.85	17.78	197.66	2.93	0.02	107.3	83.83	118.0	3.25	84.45	77.78
Standard deviations				3.01	2.23	91.66	0.55	0.03	5.6	9.93	102.8	0.77	7.47	28.24
88A00033	M	3/1	7	29.8	24.9	177.81	2.8	0.0	113.	90.8	58.	0.0	82.7	54.0
88A00031	M	3/1	7	31.3	13.7	309.77	2.8	0.08	115.	81.3	63.	3.4	133.5	61.2
88A00040	F	3/2	7	28.3	14.3	156.38	3.8	0.08	113.	82.2	63.	3.3	62.7	120.8
88A00046	F	3/2	7	26.1	14.3	143.39	3.5	0.20	113.	86.7	47.	2.1	73.6	48.8
Parameter means				28.88	16.80	196.84	3.23	0.09	113.5	85.25	57.8	2.20	88.13	71.20
Standard deviations				2.22	5.41	76.61	0.51	0.08	1.0	4.39	7.5	1.58	31.34	33.46

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	7	1.40	136.3	8.4	5.7	148.0
88A00029	M	4/1	7	1.79	152.7	10.9	7.1	156.6
88A00038	F	4/2	7	1.64	154.2	11.1	5.2	181.1
88A00041	F	4/2	7	1.71	156.1	11.4	5.5	196.0
Parameter means				1.635	149.83	10.45	5.88	170.43
Standard deviations				0.168	9.12	1.38	0.84	22.08
88A00032	M	1/1	7	1.65	149.9	10.7	7.2	161.8
88A00028	M	1/1	7	1.75	150.1	10.3	7.9	227.3
88A00043	F	1/2	7	1.40	152.2	11.2	6.0	139.7
88A00047	F	1/2	7	1.52	151.5	10.9	7.5	143.9
Parameter means				1.580	150.93	10.78	7.15	168.18
Standard deviations				0.153	1.11	0.38	0.82	40.56
88A00037	M	2/1	7	1.52	149.0	10.6	5.8	243.5
88A00035	M	2/1	7	1.46	124.7	8.1	7.4	128.7
88A00044	F	2/2	7	1.27	135.5	9.5	5.4	133.3
88A00042	F	2/2	7	1.46	143.6	10.2	6.5	144.9
Parameter means				1.428	138.20	9.60	6.28	162.60
Standard deviations				0.109	10.57	1.10	0.88	54.36
88A00033	M	3/1	7	1.77	151.1	10.6	7.6	236.3
88A00031	M	3/1	7	1.45	150.7	10.5	6.4	152.6
88A00040	F	3/2	7	1.47	146.5	10.8	6.1	126.6
88A00046	F	3/2	7	1.40	148.0	10.9	5.9	128.5
Parameter means				1.523	149.08	10.70	6.50	161.00
Standard deviations				0.168	2.20	0.18	0.76	51.58

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88A00034	M	4/1	14	0.7	45.4	4.6	0.2	5.1	26.	2.6
88A00029	M	4/1	14	0.7	21.3	5.8	0.2	5.5	33.	2.2
88A00038	F	4/2	14	1.0	32.2	5.6	0.6	4.9	36.	1.7
88A00041	F	4/2	14	0.8	27.3	5.2	0.7	4.7	48.	1.4
Parameter means				0.80	31.55	5.30	0.43	5.05	35.8	1.98
Standard deviations				0.14	10.25	0.53	0.26	0.34	9.2	0.53
88A00032	M	1/1	14	0.7	35.7	5.4	0.0	4.9	39.	1.4
88A00028	M	1/1	14	0.6	31.2	4.4	0.4	4.4	39.	2.1
88A00043	F	1/2	14	0.7	33.1	5.7	0.6	4.9	51.	2.0
88A00047	F	1/2	14	0.9	25.3	5.3	0.7	4.9	66.	1.8
Parameter means				0.73	31.33	5.20	0.43	4.78	48.8	1.83
Standard deviations				0.13	4.42	0.56	0.31	0.25	12.8	0.31
88A00037	M	2/1	14	0.7	30.4	4.7	0.2	4.8	46.	2.7
88A00035	M	2/1	14	0.8	29.0	5.2	0.0	5.2	44.	2.4
88A00044	F	2/2	14	0.8	29.1	5.0	0.4	4.3	70.	3.7
88A00042	F	2/2	14	0.8	25.9	5.4	0.4	4.8	119.	1.5
Parameter means				0.78	28.60	5.08	0.25	4.78	69.8	2.58
Standard deviations				0.05	1.91	0.30	0.19	0.37	34.9	0.91
88A00033	M	3/1	14	0.8	24.6	5.4	0.0	4.4	35.	2.5
88A00031	M	3/1	14	0.8	35.9	5.0	0.1	5.1	31.	2.3
88A00040	F	3/2	14	0.7	24.0	5.3	0.5	4.8	41.	2.6
88A00046	F	3/2	14	0.9	29.9	5.0	0.3	4.8	46.	2.5
Parameter means				0.80	28.60	5.18	0.23	4.78	38.3	2.48
Standard deviations				0.08	5.54	0.21	0.22	0.29	6.6	0.13

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDH
88A00034	M	4/1	14	32.3	11.1	228.63	3.3	0.07	113.	85.1	49.	1.9	65.5	65.9
88A00029	M	4/1	14	32.2	13.0	218.01	3.9	0.06	118.	80.9	68.	2.1	62.4	85.6
88A00038	F	4/2	14	40.2	14.2	394.59	3.5	0.09	110.	66.0	102.	1.6	67.6	209.7
88A00041	F	4/2	14	40.2	19.3	296.11	3.1	0.09	112.	66.4	189.	0.0	65.8	205.8
Parameter means				36.23	14.40	284.34	3.45	0.08	113.3	74.60	102.0	1.40	65.33	141.75
Standard deviations				4.59	3.51	81.23	0.34	0.02	3.4	9.85	62.0	0.96	2.16	76.65
88A00032	M	1/1	14	36.5	14.5	317.64	3.2	0.04	109.	71.0	55.	0.8	72.9	88.9
88A00028	M	1/1	14	40.5	12.4	356.11	3.0	0.24	104	68.1	74.	2.6	81.3	172.7
88A00043	F	1/2	14	30.3	12.3	212.41	3.8	0.0	115.	68.5	114.	0.6	90.7	154.4
88A00047	F	1/2	14	38.6	16.1	381.95	3.4	0.11	108.	67.8	82.	2.7	59.3	331.5
Parameter means				36.48	13.83	317.03	3.35	0.10	109.0	68.85	81.3	1.68	76.05	186.88
Standard deviations				4.43	1.82	74.58	0.34	0.11	4.5	1.46	24.6	1.13	13.33	102.91
88A00037	M	2/1	14	34.3	14.2	188.78	3.4	0.04	108.	74.9	90.	2.9	69.5	143.5
88A00035	M	2/1	14	41.5	12.6	253.57	3.7	0.13	115.	88.2	86.	2.2	113.5	61.3
88A00044	F	2/2	14	32.2	12.6	151.43	3.9	0.03	111.	85.5	85.	0.4	88.1	54.5
88A00042	F	2/2	14	38.6	15.8	225.02	3.3	0.0	113.	69.8	127.	0.0	95.3	110.6
Parameter means				36.65	13.80	204.70	3.58	0.05	111.8	79.60	97.0	1.38	91.60	92.48
Standard deviations				4.19	1.53	44.32	0.28	0.06	3.0	8.70	20.1	1.40	18.20	42.21
88A00033	M	3/1	14	32.9	15.0	359.01	3.8	0.0	111.	81.7	74.	1.5	64.4	53.0
88A00031	M	3/1	14	38.9	11.9	288.08	3.5	0.03	115.	80.3	100.	4.0	116.8	80.5
88A00040	F	3/2	14	23.9	17.6	147.31	3.8	0.0	112.	76.2	152.	1.8	57.7	92.3
88A00046	F	3/2	14	29.0	17.8	234.99	3.6	0.02	115.	80.5	92.	0.0	64.4	86.8
Parameter means				31.18	15.58	257.35	3.68	0.01	113.3	79.68	104.5	1.83	75.83	78.15
Standard deviations				6.33	2.76	89.23	0.15	0.02	2.1	2.40	33.5	1.65	27.50	17.45

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for COBAS I
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

PRINTED: 22-Mar-89

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88A00034	M	4/1	14	1.41	151.7	10.2	6.1	158.6
88A00029	M	4/1	14	1.66	158.0	11.5	6.0	134.2
88A00038	F	4/2	14	1.70	148.9	10.4	4.8	185.7
88A00041	F	4/2	14	1.85	152.4	10.8	4.6	173.1
Parameter means				1.655	152.75	10.73	5.38	162.90
Standard deviations				0.183	3.81	0.57	0.78	22.11
88A00032	M	1/1	14	1.30	145.4	10.9	6.0	146.4
88A00028	M	1/1	14	1.43	137.5	9.6	5.5	193.4
88A00043	F	1/2	14	1.68	149.8	10.8	5.0	139.0
88A00047	F	1/2	14	1.71	146.0	10.4	5.6	136.4
Parameter means				1.530	144.68	10.43	5.53	153.80
Standard deviations				0.198	5.16	0.59	0.41	26.74
88A00037	M	2/1	14	1.42	143.7	10.6	5.6	175.2
88A00035	M	2/1	14	1.57	156.2	11.2	6.6	163.3
88A00044	F	2/2	14	1.55	147.1	10.8	5.4	158.7
88A00042	F	2/2	14	1.70	149.2	10.6	5.5	147.6
Parameter means				1.560	149.05	10.80	5.78	161.20
Standard deviations				0.115	5.28	0.28	0.56	11.43
88A00033	M	3/1	14	1.43	149.2	10.4	5.8	225.1
88A00031	M	3/1	14	1.48	151.2	11.1	6.0	149.8
88A00040	F	3/2	14	1.77	150.5	10.2	5.3	140.2
88A00046	F	3/2	14	1.70	149.2	11.0	5.5	131.3
Parameter means				1.595	150.03	10.68	5.65	161.60
Standard deviations				0.165	0.99	0.44	0.31	43.00

Appendix H: HEMATOLOGY

List of Hematology Abbreviations/Units

RBC	Erythrocytes ($\times 10^6/\mu\text{l}$)
HGB	Hemoglobin (g/dl)
HCT	Hematocrit (%)
MCV	Mean Corpuscular Volume (femtoliters)
MCH	Mean Corpuscular Hemoglobin (picograms)
MCHC	Mean Corpuscular Hemoglobin Concentration (g/dl)
RET	Reticulocytes (%)
WBC	Total Leukocyte Count ($\times 10^3/\mu\text{l}$)
SEG	Polymorphonuclear Granulocytes (%)
BAN	Immature Neutrophils (%)
EOS	Eosinophils (%)
BAS	Basophils (%)
LYM	Lymphocytes (%)
MON	Monocytes (%)
PLT	Platelets ($\times 10^3/\mu\text{l}$)
NRBC	Nucleated Red Blood Cell (#/100 WBC)
PT	Prothrombin Time (seconds)
APPT	Activated Partial Thromboplastin Time (seconds)

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV GLP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	-13	12.0	7.13	16.6	49.2	69.0	23.3	33.7	276	4.1
88A00029	M	4/1	-13	12.3	7.31	17.2	51.2	70.1	23.5	33.6	502	4.0
88A00038	F	4/2	-12	8.6	5.99	14.3	40.8	68.1	23.9	35.0	217	2.6
88A00041	F	4/2	-12	11.0	6.75	16.5	47.7	70.7	24.4	34.6	373	2.2
Parameter means				10.98	6.80	16.15	47.23	69.48	23.78	34.23	342.0	3.23
Standard deviations				1.68	0.59	1.27	4.52	1.16	0.49	0.68	124.6	0.97
88A00032	M	1/1	-13	11.3	6.16	14.4	42.9	69.7	23.4	33.6	340	3.8
88A00028	M	1/1	-13	16.5	6.79	15.5	46.3	68.2	22.8	33.5	510	4.8
88A00043	F	1/2	-12	11.3	7.82	17.4	51.6	66.0	22.3	33.7	469	2.3
88A00047	F	1/2	-12	11.9	7.45	16.9	50.0	67.1	22.7	33.8	313	2.4
Parameter means				12.75	7.06	16.05	47.70	67.75	22.80	33.65	408.0	3.33
Standard deviations				2.52	0.73	1.36	3.89	1.58	0.45	0.13	96.2	1.20
88A00037	M	2/1	-13	11.5	6.86	15.9	47.3	68.9	23.2	33.6	318	4.0
88A00035	M	2/1	-13	10.2	7.41	15.8	48.5	65.5	21.3	32.6	562	4.5
88A00044	F	2/2	-12	13.5	8.16	18.4	55.7	68.2	22.5	33.0	350	2.1
88A00042	F	2/2	-12	14.8	6.67	15.9	46.4	69.5	23.8	34.3	375	2.0
Parameter means				12.50	7.28	16.50	49.48	68.03	22.70	33.38	401.3	3.15
Standard deviations				2.05	0.67	1.27	4.24	1.77	1.07	0.74	109.7	1.29
88A00033	M	3/1	-13	11.1	6.85	15.9	47.3	69.0	23.2	33.6	342	3.2
88A00031	M	3/1	-13	14.5	7.29	16.7	50.0	68.6	22.9	33.4	424	4.5
88A00040	F	3/2	-12	14.4	7.47	18.7	54.4	72.8	25.0	34.4	340	2.4
88A00046	F	3/2	-12	14.2	6.54	15.4	44.1	67.4	23.5	34.9	338	1.6
Parameter means				13.55	7.04	16.68	48.95	69.45	23.65	34.08	361.0	2.93
Standard deviations				1.64	0.42	1.45	4.36	2.33	0.93	0.70	42.0	1.24

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV GLP Study Number: 88003

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 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
88A00034	M	4/1	-13	41	1	0.0	0	52	6	0.0	4	6.7	17.0
88A00029	M	4/1	-13	29	0.0	9	0.0	56	6	0.0	1	8.6	14.2
88A00038	F	4/2	-12	58	2	3	0.0	35	2	0.0	0	11.8	14.2
88A00041	F	4/2	-12	42	0.0	7	0.0	43	5	3	1	6.7	13.7
Parameter means				42.5	0.8	4.8	0.0	46.5	4.8	0.8	1.5	8.45	14.78
Standard deviations				11.9	1.0	4.0	0.0	9.4	1.9	1.5	1.7	2.41	1.50
88A00032	M	1/1	-13	47	0.0	0	0.0	47	6	0.0	1	8.0	14.7
88A00028	M	1/1	-13	33	0.0	0	0.0	56	11	0.0	1	8.1	14.5
88A00043	F	1/2	-12	50	4	0.0	0	35	5	6	0.0	7.7	14.0
88A00047	F	1/2	-12	57	2	2	0.0	31	5	3	1	9.7	15.0
Parameter means				46.8	1.5	0.5	0.0	42.3	6.8	2.3	0.8	8.38	14.55
Standard deviations				10.1	1.9	1.0	0.0	11.4	2.9	2.9	0.5	0.90	0.42
88A00037	M	2/1	-13	31	0.0	0	0.0	67	2	0.0	0	6.5	16.0
88A00035	M	2/1	-13	32	1	5	0.0	55	7	0.0	0	9.5	15.7
88A00044	F	2/2	-12	62	1	1	0.0	30	3	3	0.0	5.8	13.5
88A00042	F	2/2	-12	42	0.0	2	0.0	46	7	3	2	6.8	15.2
Parameter means				41.8	0.5	2.0	0.0	49.5	4.8	1.5	0.5	7.15	15.10
Standard deviations				14.4	0.6	2.2	0.0	15.6	2.6	1.7	1.0	1.62	1.12
88A00033	M	3/1	-13	45	0.0	5	0.0	43	7	0.0	0	8.5	15.2
88A00031	M	3/1	-13	41	0.0	2	0.0	48	9	0.0	2	8.3	16.2
88A00040	F	3/2	-12	65	1	4	0.0	23	4	3	2	6.4	14.2
88A00046	F	3/2	-12	46	3	6	0.0	36	7	1	0.0	9.0	13.9
Parameter means				49.3	1.0	4.3	0.0	37.5	6.8	1.0	1.0	8.05	14.88
Standard deviations				10.7	1.4	1.7	0.0	10.8	2.1	1.4	1.2	1.14	1.04

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV
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 DOG/BEAGLE

PRINTED: 22-Mar-89

GLP Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	-6	11.1	7.36	16.7	49.5	67.3	22.7	33.7	292	3.4
88A00029	M	4/1	-6	33.4	7.27	16.9	49.7	68.4	23.2	34.0	377	3.6
88A00038	F	4/2	-7	11.8	7.23	17.4	50.8	70.3	24.1	34.3	447	3.4
88A00041	F	4/2	-7	11.5	6.82	17.3	49.6	72.7	25.4	34.9	374	2.7
Parameter means				16.95	7.17	17.08	49.90	69.68	23.85	34.23	372.5	3.28
Standard deviations				10.97	0.24	0.33	0.61	2.37	1.18	0.51	63.4	0.39
88A00032	M	1/1	-6	11.0	6.70	15.9	45.6	68.1	23.7	34.9	291	4.0
88A00028	M	1/1	-6	17.0	6.73	15.5	44.8	66.6	23.0	34.6	436	6.4
88A00043	F	1/2	-7	12.9	7.51	17.3	50.2	66.9	23.0	34.5	447	3.1
88A00047	F	1/2	-7	12.6	6.75	15.8	46.2	68.5	23.4	34.2	288	1.3
Parameter means				13.38	6.92	16.13	46.70	67.53	23.28	34.55	365.5	3.70
Standard deviations				2.56	0.39	0.80	2.40	0.92	0.34	0.29	87.9	2.12
88A00037	M	2/1	-6	13.2	6.87	16.2	47.6	69.3	23.6	34.0	427	2.8
88A00035	M	2/1	-6	9.3	7.2	15.6	46.2	64.2	21.7	33.8	435	4.1
88A00044	F	2/2	-7	11.4	7.64	18.2	53.6	70.1	23.8	34.0	325	2.6
88A00042	F	2/2	-7	14.9	6.84	16.8	49.0	71.7	24.6	34.3	403	2.0
Parameter means				12.20	7.14	16.70	49.10	68.83	23.43	34.03	397.5	2.88
Standard deviations				2.40	0.37	1.11	3.21	3.24	1.23	0.21	50.2	0.88
88A00033	M	3/1	-6	9.6	6.81	15.9	46.0	67.5	23.3	34.6	273	4.3
88A00031	M	3/1	-6	16.9	6.77	15.6	46.0	68.0	23.0	33.9	367	4.2
88A00040	F	3/2	-7	11.6	7.21	18.9	53.6	74.4	26.2	35.3	323	3.4
88A00046	F	3/2	-7	10.4	5.82	14.1	40.2	69.1	24.2	35.1	172	1.7
Parameter means				12.13	6.65	16.13	46.45	69.75	24.18	34.73	283.8	3.40
Standard deviations				3.29	0.59	2.01	5.50	3.17	1.44	0.62	83.8	1.20

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
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PRINTED: 22-Mar-89

GLP Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
88A00034	M	4/1	-6	56	1	0.0	0	32	8	3	0.0	6.5	15.2
88A00029	M	4/1	-6	53	4	3	0	30	4	6	2	8.5	16.0
88A00038	F	4/2	-7	50	2	2	0.0	37	8	1	1	11.0	NT
88A00041	F	4/2	-7	50	0.0	5	0.0	31	3	11	0.0	9.0	13.7
Parameter means				52.3	1.8	2.5	0.0	32.5	5.8	5.3	0.8	8.75	14.97
Standard deviations				2.9	1.7	2.1	0.0	3.1	2.6	4.3	1.0	1.85	1.17
88A00032	M	1/1	-6	63	0.0	0	0.0	30	3	4	3	NT	NT
88A00028	M	1/1	-6	49	2	0.0	0	38	5	6	0.0	8.0	16.0
88A00043	F	1/2	-7	55	1	3	0.0	27	6	8	0.0	7.5	13.5
88A00047	F	1/2	-7	59	2	4	0.0	23	9	3	3	8.5	13.7
Parameter means				56.5	1.3	1.8	0.0	29.5	5.8	5.3	1.5	7.75	16.13
Standard deviations				6.0	1.0	2.1	0.0	6.4	2.5	2.2	1.7	0.65	3.63
88A00037	M	2/1	-6	50	0.0	0	0.0	45	2	3	0.0	7.5	15.7
88A00035	M	2/1	-6	46	0.0	11	0.0	27	7	9	1	8.1	14.7
88A00044	F	2/2	-7	54	3	2	1	34	6	0.0	0	9.0	12.7
88A00042	F	2/2	-7	44	1	10	0.0	42	1	2	0.0	6.5	12.5
Parameter means				48.5	1.0	5.8	0.3	37.0	4.0	3.5	0.3	7.78	13.90
Standard deviations				4.4	1.4	5.6	0.5	8.1	2.9	3.9	0.5	1.05	1.56
88A00033	M	3/1	-6	64	3	5	0.0	15	10	3	0.0	5.5	17.0
88A00031	M	3/1	-6	55	1	2	0.0	29	9	4	0.0	NT	NT
88A00040	F	3/2	-7	50	2	7	1	31	3	6	1	7.0	13.2
88A00046	F	3/2	-7	51	0.0	6	0.0	37	3	3	3	6.8	12.7
Parameter means				55.0	1.5	5.0	0.3	28.0	6.3	4.0	1.0	6.43	14.3
Standard deviations				6.4	1.3	2.2	0.5	9.3	3.8	1.4	1.4	.81	2.35

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/3EAGLE

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

PRINTED: 22-Mar-89

Animal Number	Sex	Group/ Subgroup	Day of Study*	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	0	9.5	6.79	15.6	45.3	66.7	23.0	34.4	270	1.7
88A00029	M	4/1	0	15.2	7.5	18.4	52.1	69.4	24.5	35.3	403	2.4
88A00038	F	4/2	0	10.4	6.61	16.5	46.5	70.4	25.0	35.5	412	1.4
88A00041	F	4/2	0	12.3	5.87	14.9	42.8	72.9	25.4	34.8	354	1.2
Parameter means				11.85	6.69	16.35	46.68	69.85	24.48	35.00	359.8	1.68
Standard deviations				2.52	0.67	1.52	3.93	2.56	1.05	0.50	65.0	0.53
88A00032	M	1/1	0	8.2	6.00	14.6	41.9	69.8	24.3	34.8	300	3.3
88A00028	M	1/1	0	25.9	6.74	16.0	44.8	66.4	23.7	35.7	395	5.0
88A00043	F	1/2	0	12.9	7.24	17.4	49.2	67.9	24.0	35.4	443	3.3
88A00047	F	1/2	0	12.6	6.51	15.4	44.4	68.2	23.7	34.7	330	1.0
Parameter means				14.90	6.62	15.85	45.08	68.08	23.93	35.15	367.0	3.15
Standard deviations				7.64	0.51	1.18	3.03	1.39	0.29	0.48	64.3	1.64
88A00037	M	2/1	0	12.8	5.94	14.7	42.7	71.9	24.7	34.4	230	2.4
88A00035	M	2/1	0	9.8	6.96	15.5	44.2	63.5	22.3	35.1	379	2.8
88A00044	F	2/2	0	10.7	7.27	17.3	51.1	70.3	23.8	33.9	305	1.0
88A00042	F	2/2	0	12.6	6.52	15.9	46.9	71.9	24.4	33.9	375	1.8
Parameter means				11.48	6.67	15.85	46.23	69.40	23.80	34.33	322.3	2.00
Standard deviations				1.46	0.58	1.09	3.69	4.00	1.07	0.57	70.3	0.78
88A00033	M	3/1	0	10.9	6.57	15.4	45.4	69.1	23.4	33.9	296	3.8
88A00031	M	3/1	0	15.6	6.89	16.2	47.1	68.3	23.5	34.4	373	2.6
88A00040	F	3/2	0	11.8	6.64	17.3	49.7	74.8	26.1	34.8	312	1.2
88A00046	F	3/2	0	9.0	5.62	13.4	38.8	69.0	23.8	34.5	295	1.4
Parameter means				11.83	6.43	15.58	45.25	70.30	24.20	34.40	319.0	2.25
Standard deviations				2.77	0.56	1.65	4.65	3.02	1.28	0.37	36.8	1.20

* Day 0 refers to pretreatment samples taken on the day of dosing.

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV GLP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study*	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
88A00034	M	4/1	0	44	6	1	0.0	42	3	4	0.0	NT	NT
88A00029	M	4/1	0	38	0.0	7	0.0	41	3	11	0.0	NT	NT
88A00038	F	4/2	0	54	0.0	5	0.0	32	8	1	0.0	10.3	12.5
88A00041	F	4/2	0	55	0.0	6	0.0	29	7	3	0.0	6.7	12.2
Parameter means				47.8	1.5	4.8	0.0	36.0	5.3	4.8	0.0	8.5	12.35
Standard deviations				8.2	3.0	2.6	0.0	6.5	2.6	4.3	0.0	2.55	0.21
88A00032	M	1/1	0	62	5	6	0.0	17	7	0.0	0	8.0	19.0
88A00028	M	1/1	0	59	6	0.0	0	27	3	5	0.0	8.0	12.0
88A00043	F	1/2	0	55	0.0	6	0.0	29	6	4	0.0	5.8	12.7
88A00047	F	1/2	0	54	0.0	9	0.0	29	5	3	0.0	7.8	13.5
Parameter means				57.5	2.8	5.3	0.0	25.5	5.3	3.0	0.0	7.40	14.3
Standard deviations				3.7	3.2	3.8	0.0	5.7	1.7	2.2	0.0	1.07	3.19
88A00037	M	2/1	0	66	1	0.0	0	28	4	1	0.0	NT	NT
88A00035	M	2/1	0	54	0.0	2	0.0	40	4	0.0	0	7.5	38.7
88A00044	F	2/2	0	60	0.0	0	0.0	26	7	7	0.0	5.7	14.5
88A00042	F	2/2	0	46	1	2	0.0	41	7	3	0.0	7.2	12.7
Parameter means				56.5	0.5	1.0	0.0	33.8	5.5	2.8	0.0	6.80	21.97
Standard deviations				8.5	0.6	1.2	0.0	7.8	1.7	3.1	0.0	0.96	14.52
88A00033	M	3/1	0	63	0.0	0	0.0	35	1	1	0.0	NT	NT
88A00031	M	3/1	0	61	2	0.0	0	35	1	1	0.0	7.3	14.2
88A00040	F	3/2	0	49	1	4	0.0	40	6	0.0	0	8.5	13.7
88A00046	F	3/2	0	44	0.0	1	0.0	50	2	3	0.0	6.8	14.0
Parameter means				54.3	0.8	1.3	0.0	40.0	2.5	1.3	0.0	7.53	13.97
Standard deviations				9.2	1.0	1.9	0.0	7.1	2.4	1.3	0.0	0.87	0.25

* Day 0 refers to pretreatment samples taken on the day of dosing.

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

GLP Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

PRINTED: 22-Mar-89

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	0/6hr	12.4	6.60	15.4	45.1	68.4	23.3	34.1	281	1.3
88A00029	M	4/1	0/6hr	15.2	6.59	18.2	45.7	69.4	27.6	39.8	384	1.7
88A00038	F	4/2	0/6hr	11.1	6.59	15.6	45.8	69.5	23.7	34.1	399	1.0
88A00041	F	4/2	0/6hr	12.3	6.53	16.6	46.9	71.8	25.4	35.4	298	3.1
Parameter means				12.75	6.58	16.45	45.88	69.78	25.00	35.85	340.5	1.78
Standard deviations				1.74	0.03	1.28	0.75	1.44	1.96	2.70	59.6	0.93
88A00032	M	1/1	0/6hr	10.0	5.78	13.9	40.3	69.8	24.0	34.5	263	2.0
88A00028	M	1/1	0/6hr	27.2	6.29	14.5	43.5	69.1	23.1	33.3	337	3.2
88A00043	F	1/2	0/6hr	13.5	6.78	15.9	46.4	68.4	23.5	34.3	379	1.7
88A00047	F	1/2	0/6hr	15.8	6.25	14.3	43.9	70.2	22.9	32.6	279	1.6
Parameter means				16.63	6.28	14.65	43.53	69.38	23.38	33.68	314.5	2.13
Standard deviations				7.44	0.41	0.87	2.50	0.79	0.49	0.89	53.5	0.74
88A00037	M	2/1	0/6hr	14.6	6.09	14.5	43.7	71.8	23.8	33.2	335	1.4
88A00035	M	2/1	0/6hr	16.0	7.42	16.2	48.6	65.5	21.8	33.3	395	3.4
88A00044	F	2/2	0/6hr	14.1	7.2	16.9	51.5	71.5	23.5	32.8	327	1.6
88A00042	F	2/2	0/6hr	16.9	6.71	16.2	48.8	72.7	24.1	33.2	389	1.0
Parameter means				15.40	6.86	15.95	48.15	70.38	23.30	33.13	361.5	1.85
Standard deviations				1.28	0.59	1.02	3.25	3.29	1.03	0.22	35.5	1.06
88A00033	M	3/1	0/6hr	11.5	6.00	14.6	40.8	68.0	24.3	35.8	260	1.3
88A00031	M	3/1	0/6hr	15.2	6.42	14.9	44.5	69.3	23.2	33.5	316	2.8
88A00040	F	3/2	0/6hr	10.6	6.55	17.0	48.3	73.8	26.0	35.2	323	1.3
88A00046	F	3/2	0/6hr	9.3	6.1	14.4	41.5	68.1	23.6	34.7	307	1.0
Parameter means				11.65	6.27	15.23	43.78	69.80	24.28	34.80	301.5	1.60
Standard deviations				2.53	0.26	1.20	3.42	2.73	1.24	0.98	28.4	0.81

ACUTE/ACUTE INTRAVENOUS

Study Start Date: 27-Sep-88

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
888A00034	M	4/1	0/6hr	42	1	2	0.0	46	2	6	0.0	10.0	15.0
888A00029	M	4/1	0/6hr	37	0.0	6	0.0	47	3	7	0.0	7.0	17.5
888A00038	F	4/2	0/6hr	51	1	1	0.0	39	3	5	0.0	12.2	15.3
888A00041	F	4/2	0/6hr	39	0.0	2	0.0	55	2	2	0.0	7.7	49.2
Parameter means				42.3	0.5	2.8	0.0	46.8	2.5	5.0	0.0	9.23	24.25
Standard deviations				6.2	0.6	2.2	0.0	6.6	0.6	2.2	0.0	2.36	16.67
888A00032	M	1/1	0/6hr	72	0.0	1	0.0	24	1	1	0.0	6.5	12.0
888A00028	M	1/1	0/6hr	77	0.0	1	0.0	12	8	1	1	7.5	14.7
888A00043	F	1/2	0/6hr	74	0.0	0	0.0	20	5	1	0.0	8.4	17.0
888A00047	F	1/2	0/6hr	82	0.0	3	0.0	9	6	0.0	0	9.3	18.3
Parameter means				76.3	0.0	1.3	0.0	16.3	5.0	0.8	0.3	7.93	15.50
Standard deviations				4.3	0.0	1.3	0.0	6.9	2.9	0.5	0.5	1.20	2.77
888A00037	M	2/1	0/6hr	76	0.0	0	0.0	19	5	0.0	0	8.8	14.2
888A00035	M	2/1	0/6hr	58	1	0.0	0	31	6	4	0.0	7.8	15.5
888A00044	F	2/2	0/6hr	75	1	1	0.0	13	5	0.0	0	8.3	15.5
888A00042	F	2/2	0/6hr	72	1	1	0.0	15	7	4	0.0	8.2	16.8
Parameter means				70.3	0.8	0.5	0.0	19.5	5.8	2.0	0.0	8.28	15.50
Standard deviations				8.3	0.5	0.6	0.0	8.1	1.0	2.3	0.0	0.41	1.06
888A00033	M	3/1	0/6hr	66	0.0	9	0.0	20	2	1	0.0	7.3	14.7
888A00031	M	3/1	0/6hr	60	2	2	0.0	32	3	1	0.0	7.7	15.7
888A00040	F	3/2	0/6hr	62	0.0	3	0.0	26	6	3	0.0	8.9	20.2
888A00046	F	3/2	0/6hr	46	0.0	3	0.0	48	3	0.0	0	9.8	20.3
Parameter means				58.5	0.5	4.3	0.0	31.5	3.5	1.3	0.0	8.43	17.73
Standard deviations				8.7	1.0	3.2	0.0	12.0	1.7	1.3	0.0	1.14	2.94

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV GLP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	1/24hr	17.3	6.9	14.2	41.8	68.7	23.3	34.0	239	1.4
88A00029	M	4/1	1/24hr	13.9	6.91	16.6	48.2	69.8	24.0	34.4	391	1.8
88A00038	F	4/2	1/24hr	9.9	7.19	17.0	50.4	70.1	23.6	33.7	418	1.4
88A00041	F	4/2	1/24hr	9.6	6.05	15.6	44.1	72.9	25.8	35.4	339	1.3
Parameter means				12.68	6.76	15.85	46.13	70.38	24.18	34.38	346.8	1.48
Standard deviations				3.65	0.49	1.25	3.89	1.79	1.12	0.74	79.0	0.22
88A00032	M	1/1	1/24hr	7.7	5.97	14.2	41.5	69.5	23.8	34.2	281	2.0
88A00028	M	1/1	1/24hr	19.1	6.09	14.4	41.2	67.7	23.6	35.0	323	1.9
88A00043	F	1/2	1/24hr	10.0	7.19	16.9	48.7	67.8	23.5	34.7	398	1.6
88A00047	F	1/2	1/24hr	11.2	6.55	15.6	45.2	69.0	23.8	34.5	306	2.3
Parameter means				12.00	6.45	15.28	44.15	68.50	23.68	34.60	327.0	1.95
Standard deviations				4.95	0.55	1.25	3.54	0.89	0.15	0.34	50.4	0.29
88A00037	M	2/1	1/24hr	10.1	5.85	14.2	41.5	71.0	24.3	34.2	316	1.0
88A00035	M	2/1	1/24hr	8.0	6.98	15.4	45.7	65.5	22.1	33.7	379	2.3
88A00044	F	2/2	1/24hr	9.8	7.01	16.6	49.2	70.2	23.7	33.7	289	0.6
88A00042	F	2/2	1/24hr	12.3	6.49	15.7	46.5	71.6	24.2	33.8	365	1.2
Parameter means				10.05	6.58	15.48	45.73	69.58	23.58	33.85	337.3	1.28
Standard deviations				1.76	0.54	0.99	3.19	2.78	1.02	0.24	42.0	0.73
88A00033	M	3/1	1/24hr	9.1	6.42	15.3	44.4	69.1	23.8	34.5	284	1.7
88A00031	M	3/1	1/24hr	15.8	6.41	15.5	44.4	69.3	24.2	34.9	350	2.3
88A00040	F	3/2	1/24hr	10.6	6.20	16.7	46.3	74.6	26.9	36.1	280	1.0
88A00046	F	3/2	1/24hr	9.6	6.06	14.4	41.5	68.5	23.8	34.7	279	1.0
Parameter means				11.28	6.27	15.48	44.15	70.38	24.68	35.05	298.3	1.50
Standard deviations				3.08	0.17	0.95	1.98	2.84	1.50	0.72	34.6	0.63

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

GLP Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
88A00034	M	4/1	1/24hr	67	1	0.0	0	27	4	1	0.0	8.6	12.2
88A00029	M	4/1	1/24hr	42	0.0	4	0.0	44	5	5	1	7.0	12.7
88A00038	F	4/2	1/24hr	62	0.0	6	0.0	26	2	4	0.0	12.0	18.5
88A00041	F	4/2	1/24hr	41	0.0	7	0.0	42	4	5	0.0	7.8	20.1
Parameter means				53.0	0.3	4.3	0.0	34.8	3.8	3.8	0.3	8.85	15.88
Standard deviations				13.4	0.5	3.1	0.0	9.6	1.3	1.9	0.5	2.20	4.01
88A00032	M	1/1	1/24hr	54	0.0	7	0.0	29	8	2	0.0	6.5	12.0
88A00028	M	1/1	1/24hr	62	1	0.0	0	29	7	1	1	6.0	11.2
88A00043	F	1/2	1/24hr	60	1	1	0.0	35	3	0.0	0	7.3	18.0
88A00047	F	1/2	1/24hr	74	0.0	8	0.0	13	5	0.0	2	8.5	26.3
Parameter means				62.5	0.5	4.0	0.0	26.5	5.8	0.8	0.8	7.08	16.88
Standard deviations				8.4	0.6	4.1	0.0	9.4	2.2	1.0	1.0	1.09	6.98
88A00037	M	2/1	1/24hr	69	1	0.0	0	27	3	0.0	0	7.0	12.7
88A00035	M	2/1	1/24hr	61	2	3	0.0	22	9	3	0.0	6.3	12.5
88A00044	F	2/2	1/24hr	51	1	3	0.0	33	3	9	0.0	7.7	23.7
88A00042	F	2/2	1/24hr	48	0.0	5	0.0	37	8	2	0.0	7.5	27.5
Parameter means				57.3	1.0	2.8	0.0	29.8	5.8	3.5	0.0	7.13	19.10
Standard deviations				9.6	0.8	2.1	0.0	6.6	3.2	3.9	0.0	0.62	7.66
88A00033	M	3/1	1/24hr	63	0.0	15	0.0	14	5	3	0.0	5.5	15.0
88A00031	M	3/1	1/24hr	46	0.0	5	0.0	40	6	3	0.0	7.0	13.2
88A00040	F	3/2	1/24hr	55	0.0	1	0.0	28	6	10	0.0	9.2	17.3
88A00046	F	3/2	1/24hr	47	0.0	2	0.0	41	6	4	0.0	9.0	19.7
Parameter means				52.8	0.0	5.8	0.0	30.8	5.8	5.0	0.0	7.68	16.30
Standard deviations				7.9	0.0	6.4	0.0	12.6	0.5	3.4	0.0	1.76	2.82

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

GLP Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	2/48hr	14.4	6.48	15.3	44.4	68.5	23.6	34.5	244	1.5
88A00029	M	4/1	2/48hr	21.6	6.48	15.0	43.9	67.7	23.1	34.2	412	2.5
88A00038	F	4/2	2/48hr	9.6	6.68	15.8	46.0	68.9	23.7	34.3	380	0.5
88A00041	F	4/2	2/48hr	10.5	6.24	15.8	44.9	71.9	25.3	35.2	299	1.5
Parameter means				14.03	6.47	15.48	44.80	69.25	23.93	34.55	333.8	1.50
Standard deviations				5.46	0.18	0.39	0.90	1.84	0.95	0.45	76.4	0.82
88A00032	M	1/1	2/48hr	9.8	5.94	14.4	41.0	69.1	24.2	35.1	284	1.6
88A00028	M	1/1	2/48hr	2.1	6.56	15.0	44.3	67.5	22.9	33.9	393	2.4
88A00043	F	1/2	2/48hr	10.9	7.30	16.7	48.9	67.0	22.9	34.2	376	0.5
88A00047	F	1/2	2/48hr	10.0	6.92	15.9	47.3	68.4	23.0	33.6	311	2.7
Parameter means				8.21	6.68	15.50	45.38	68.00	23.25	34.20	341.0	1.80
Standard deviations				4.07	0.58	1.01	3.48	0.93	0.64	0.65	51.9	0.98
88A00037	M	2/1	2/48hr	9.6	5.94	14.4	41.7	70.2	24.2	34.5	366	1.0
88A00035	M	2/1	2/48hr	10.4	6.85	15.3	44.3	64.6	22.3	34.5	388	4.0
88A00044	F	2/2	2/48hr	9.9	6.96	16.7	48.2	69.3	24.0	34.6	290	0.8
88A00042	F	2/2	2/48hr	11.5	6.32	15.6	44.9	71.1	24.7	34.7	358	0.7
Parameter means				10.35	6.52	15.50	44.78	68.80	23.80	34.58	350.5	1.63
Standard deviations				0.83	0.48	0.95	2.67	2.89	1.04	0.10	42.3	1.59
88A00033	M	3/1	2/48hr	10.7	6.36	15.0	43.9	69.0	23.6	34.2	294	1.5
88A00031	M	3/1	2/48hr	17.0	6.56	15.6	45.4	69.2	23.8	34.4	301	2.1
88A00040	F	3/2	2/48hr	12.2	6.74	17.5	49.6	73.6	26.0	35.3	303	0.4
88A00046	F	3/2	2/48hr	10.7	6.53	15.3	44.9	68.7	23.4	34.1	282	0.9
Parameter means				12.65	6.55	15.85	45.98	70.13	24.20	34.50	295.0	1.23
Standard deviations				2.98	0.16	1.13	2.51	2.33	1.21	0.55	9.5	0.74

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

GLP Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
88A00034	M	4/1	2/48hr	51	0.0	2	0.0	40	6	1	0.0	8.0	15.5
88A00029	M	4/1	2/48hr	40	1	11	0.0	32	6	0.0	0	7.2	13.2
88A00038	F	4/2	2/48hr	39	1	3	0.0	52	5	1	0.0	12.8	17.5
88A00041	F	4/2	2/48hr	46	0.0	8	0.0	40	3	3	0.0	7.3	16.3
Parameter means				44.0	0.5	6.0	0.0	41.0	5.0	1.3	0.0	8.83	15.63
Standard deviations				5.6	0.6	4.2	0.0	8.2	1.4	1.3	0.0	2.67	1.81
88A00032	M	1/1	2/48hr	57	0.0	4	0.0	30	6	3	0.0	8.2	16.5
88A00028	M	1/1	2/48hr	63	0.0	1	0.0	18	8	10	2	7.5	16.9
88A00043	F	1/2	2/48hr	62	0.0	1	0.0	32	3	2	0.0	8.5	20.5
88A00047	F	1/2	2/48hr	71	0.0	6	0.0	17	4	2	0.0	13.2	19.5
Parameter means				63.3	0.0	3.0	0.0	24.3	5.3	4.3	0.5	9.35	18.35
Standard deviations				5.8	0.0	2.4	0.0	7.8	2.2	3.0	1.0	2.60	1.96
88A00037	M	2/1	2/48hr	61	0.0	1	0.0	28	6	4	0.0	8.0	14.0
88A00035	M	2/1	2/48hr	55	1	1	0.0	37	5	1	0.0	7.7	27.2
88A00044	F	2/2	2/48hr	51	0.0	1	0.0	46	0.0	2	0.0	8.0	18.0
88A00042	F	2/2	2/48hr	52	0.0	8	0.0	40	0.0	0	0.0	8.0	32.3
Parameter means				54.8	0.3	2.8	0.0	37.8	2.8	1.8	0.0	7.93	22.88
Standard deviations				4.5	0.5	3.5	0.0	7.5	3.2	1.7	0.0	0.15	8.37
88A00033	M	3/1	2/48hr	55	0.0	8	0.0	22	10	4	0.0	7.5	12.2
88A00031	M	3/1	2/48hr	57	2	1	0.0	31	9	0.0	0	8.0	16.0
88A00040	F	3/2	2/48hr	62	0.0	3	0.0	25	4	6	0.0	10.0	17.3
88A00046	F	3/2	2/48hr	41	0.0	2	0.0	50	6	1	0.0	9.5	22.5
Parameter means				53.8	0.5	3.5	0.0	32.0	7.3	2.8	0.0	8.75	17.00
Standard deviations				9.0	1.0	3.1	0.0	12.6	2.8	2.8	0.0	1.19	4.26

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
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PRINTED: 22-Mar-89

GLP Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	3/72hr	10.1	6.46	15.3	44.1	68.2	23.7	34.7	231	4.7
88A00029	M	4/1	3/72hr	13.4	6.86	16.2	47.8	69.7	23.6	33.9	410	2.4
88A00038	F	4/2	3/72hr	9.8	6.76	15.9	47.3	70.0	23.5	33.6	378	0.5
88A00041	F	4/2	3/72hr	11.1	6.09	15.7	44.3	72.8	25.8	35.4	395	1.4
Parameter means				11.10	6.54	15.78	45.88	70.18	24.15	34.40	353.5	2.25
Standard deviations				1.63	0.35	0.38	1.95	1.92	1.10	0.81	82.7	1.81
88A00032	M	1/1	3/72hr	9.3	6.33	15.0	43.4	68.5	23.7	34.6	293	1.2
88A00028	M	1/1	3/72hr	21.4	6.64	14.9	44.8	67.5	22.4	33.3	385	1.4
88A00043	F	1/2	3/72hr	12.2	7.09	16.9	47.9	67.5	23.8	35.3	429	1.5
88A00047	F	1/2	3/72hr	10.1	6.16	14.7	42.1	68.3	23.9	34.9	313	1.0
Parameter means				13.25	6.56	15.38	44.55	67.95	23.45	34.53	355.0	1.28
Standard deviations				5.57	0.41	1.02	2.49	0.53	0.70	0.87	63.2	0.22
88A00037	M	2/1	3/72hr	12.7	6.42	15.5	44.9	70.0	24.1	34.5	370	1.5
88A00035	M	2/1	3/72hr	7.2	6.81	15.3	44.0	64.6	22.5	34.8	378	1.7
88A00044	F	2/2	3/72hr	9.5	6.79	16.3	47.7	70.2	24.0	34.2	330	0.8
88A00042	F	2/2	3/72hr	11.6	6.71	16.7	47.7	71.1	24.9	35.0	434	2.6
Parameter means				10.25	6.68	15.95	46.08	68.98	23.88	34.63	378.0	1.65
Standard deviations				2.43	0.18	0.66	1.91	2.96	1.00	0.35	42.8	0.74
88A00033	M	3/1	3/72hr	9.1	6.57	15.5	44.9	68.3	23.6	34.5	251	2.1
88A00031	M	3/1	3/72hr	15.6	6.60	15.4	45.5	68.9	23.3	33.8	343	3.8
88A00040	F	3/2	3/72hr	12.8	6.53	17.2	49.0	75.0	26.3	35.1	322	0.8
88A00046	F	3/2	3/72hr	10.9	6.29	15.6	43.5	69.1	24.8	35.9	307	0.4
Parameter means				12.10	6.50	15.93	45.73	70.33	24.50	34.83	305.8	1.78
Standard deviations				2.78	0.14	0.85	2.34	3.14	1.36	0.89	39.4	1.53

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV GLP Study Number: 88003
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ICUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
88A00034	M	4/1	3/72hr	46	0.0	0	0.0	44	9	1	0.0	6.6	14.4
88A00029	M	4/1	3/72hr	NT	NT	NT	NT	NT	NT	NT	NT	7.7	11.7
88A00038	F	4/2	3/72hr	55	0.0	3	0.0	37	0.0	5	0.0	12.0	17.7
88A00041	F	4/2	3/72hr	43	1	5	0.0	43	7	1	0.0	7.5	17.0
Parameter means				48.0	0.3	2.7	0.0	41.3	5.3	2.3	0.0	8.45	15.20
Standard deviations				6.2	0.6	2.5	0.0	3.8	4.7	2.3	0.0	2.41	2.73
88A00032	M	1/1	3/72hr	52	0.0	9	0.0	27	5	7	0.0	6.7	12.7
88A00028	M	1/1	3/72hr	NT	NT	NT	NT	NT	NT	NT	NT	6.8	11.2
88A00043	F	1/2	3/72hr	56	0.0	4	0.0	38	1	1	0.0	8.0	17.5
88A00047	F	1/2	3/72hr	62	1	7	0.0	20	8	2	0.0	9.0	17.0
Parameter means				56.7	0.3	6.7	0.0	28.3	4.7	3.3	0.0	7.63	14.60
Standard deviations				5.0	0.6	2.5	0.0	9.1	3.5	3.2	0.0	1.09	3.13
88A00037	M	2/1	3/72hr	59	3	1	0.0	30	7	0.0	0	6.0	12.2
88A00035	M	2/1	3/72hr	46	1	3	0.0	44	3	3	0.0	14.8	21.5
88A00044	F	2/2	3/72hr	47	0.0	1	0.0	49	2	1	0.0	8.5	18.7
88A00042	F	2/2	3/72hr	35	0.0	7	0.0	54	3	1	0.0	7.9	18.0
Parameter means				46.8	1.0	3.0	0.0	44.3	3.8	1.3	0.0	9.30	17.60
Standard deviations				9.8	1.4	2.8	0.0	10.3	2.2	1.3	0.0	3.82	3.90
88A00033	M	3/1	3/72hr	51	0.0	11	0.0	32	3	3	0.0	6.5	12.2
88A00031	M	3/1	3/72hr	70	6	3	0.0	13	8	0.0	0	8.9	11.2
88A00040	F	3/2	3/72hr	58	0.0	1	0.0	31	4	5	0.0	8.2	16.1
88A00046	F	3/2	3/72hr	50	0.0	2	0.0	45	2	1	0.0	8.0	17.5
Parameter means				57.3	1.5	4.3	0.0	30.3	4.3	2.3	0.0	7.90	14.25
Standard deviations				9.2	3.0	4.6	0.0	13.1	2.6	2.2	0.0	1.01	3.03

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH Expanded Statistical Table for BAKER I
 DIV OF RES SUPP, PATH SERV GLP Study Number: 88003
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 DOG/BEAGLE

PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	7	11.5	6.4	15.0	43.7	68.3	23.4	34.3	250	1.1
88A00029	M	4/1	7	15.2	6.64	16.1	46.4	69.9	24.2	34.7	379	3.3
88A00038	F	4/2	7	9.8	6.96	16.2	49.0	70.4	23.3	33.1	418	0.8
88A00041	F	4/2	7	13.2	6.68	16.6	48.9	73.2	24.9	33.9	289	2.6
Parameter means				12.43	6.67	15.98	47.00	70.45	23.95	34.00	334.0	1.95
Standard deviations				2.31	0.23	0.68	2.51	2.04	0.75	0.68	77.8	1.20
88A00032	M	1/1	7	9.0	5.53	13.6	38.1	68.9	24.6	35.7	276	2.1
88A00028	M	1/1	7	22.5	6.36	14.9	43.1	67.7	23.4	34.6	438	4.5
88A00043	F	1/2	7	13.6	7.5	16.5	50.6	67.4	22.0	32.6	444	1.8
88A00047	F	1/2	7	9.6	6.71	15.4	46.0	68.6	23.0	33.5	294	1.2
Parameter means				13.68	6.53	15.10	44.45	68.15	23.25	34.10	363.0	2.40
Standard deviations				6.23	0.82	1.20	5.24	0.71	1.08	1.34	90.4	1.45
88A00037	M	2/1	7	12.2	6.48	15.7	45.9	70.8	24.2	34.2	375	2.2
88A00035	M	2/1	7	16.8	6.74	14.6	43.7	64.8	21.7	33.4	330	2.7
88A00044	F	2/2	7	10.3	7.09	16.2	49.8	70.3	22.8	32.5	295	1.2
88A00042	F	2/2	7	13.0	6.18	15.3	44.3	71.7	24.8	34.5	365	0.5
Parameter means				13.08	6.62	15.45	45.93	69.40	23.38	33.65	341.3	1.65
Standard deviations				2.73	0.39	0.68	2.75	3.12	1.40	0.90	36.4	0.99
88A00033	M	3/1	7	11.1	6.28	15.2	43.6	69.5	24.2	34.9	296	5.2
88A00031	M	3/1	7	13.3	6.51	15.5	44.5	68.4	23.8	34.8	325	4.7
88A00040	F	3/2	7	10.8	7.07	17.5	52.5	74.3	24.8	33.3	282	0.5
88A00046	F	3/2	7	10.3	6.42	15.2	44.4	69.1	23.7	34.2	285	0.8
Parameter means				11.38	6.57	15.85	46.25	70.33	24.13	34.30	297.0	2.80
Standard deviations				1.33	0.35	1.11	4.19	2.69	0.50	0.73	19.6	2.49

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ACUTE/ACUTE INTRAVENOUS

Study Start Date: 27-Sep-88

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
888A00034	M	4/1	7	50	0.0	5	0.0	36	5	4	2	7.1	26.9
888A00029	M	4/1	7	40	0.0	6	0.0	47	1	6	0.0	6.5	13.2
888A00038	F	4/2	7	61	1	2	0.0	34	2	0.0	0	11.5	16.0
888A00041	F	4/2	7	51	0.0	7	0.0	34	7	1	0.0	7.2	18.7
Parameter means				50.5	0.3	5.0	0.0	37.8	3.8	2.8	0.5	8.08	18.7
Standard deviations				8.6	0.5	2.2	0.0	6.2	2.8	2.8	1.0	2.3	5.91
888A00032	M	1/1	7	50	1	3	0.0	42	2	2	0.0	7.5	13.0
888A00028	M	1/1	7	58	1	1	0.0	30	3	7	1	NT	13.2
888A00043	F	1/2	7	50	0.0	1	0.0	46	3	0.0	0	8.0	17.5
888A00047	F	1/2	7	58	0.0	3	0.0	35	4	0.0	0	8.0	26.1
Parameter means				54.0	0.5	2.0	0.0	38.3	3.0	2.3	0.3	7.83	17.45
Standard deviations				4.6	0.6	1.2	0.0	7.1	0.8	3.3	0.5	0.29	6.13
888A00037	M	2/1	7	70	0.0	1	0.0	24	3	2	0.0	6.5	15.2
888A00035	M	2/1	7	68	2	2	0.0	24	3	1	0.0	6.8	13.7
888A00044	F	2/2	7	45	1	2	0.0	49	2	1	0.0	8.8	17.0
888A00042	F	2/2	7	52	0.0	3	0.0	43	1	1	0.0	7.5	16.0
Parameter means				58.8	0.8	2.0	0.0	35.0	2.3	1.3	0.0	7.40	15.48
Standard deviations				12.2	1.0	0.8	0.0	12.9	1.0	0.5	0.0	1.02	1.39
888A00033	M	3/1	7	49	1	10	0.0	34	3	3	2	7.3	12.2
888A00031	M	3/1	7	41	1	2	0.0	51	1	4	0.0	6.5	15.0
888A00040	F	3/2	7	61	1	1	0.0	28	4	5	0.0	8.0	15.7
888A00046	F	3/2	7	56	1	1	0.0	36	4	2	0.0	7.5	20.0
Parameter means				51.8	1.0	3.5	0.0	37.3	3.0	3.5	0.5	7.33	15.73
Standard deviations				8.7	0.0	4.4	0.0	9.8	1.4	1.3	1.0	0.62	3.23

Appendix H (cont.): HEMATOLOGY

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PRINTED: 22-Mar-89

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET
88A00034	M	4/1	14	9.8	5.65	12.9	38.8	68.6	22.8	33.2	284	0.9
88A00029	M	4/1	14	11.2	6.74	15.5	47.1	69.9	23.0	32.9	366	0.7
88A00038	F	4/2	14	10.0	6.85	18.2	48.2	70.3	26.6	37.8	389	1.9
88A00041	F	4/2	14	12.5	6.27	15.6	46.1	73.6	24.9	33.8	341	1.2
Parameter means				10.88	6.38	15.55	45.05	70.60	24.33	34.43	345.0	1.18
Standard deviations				1.25	0.55	2.16	4.25	2.13	1.79	2.28	45.1	0.53
88A00032	M	1/1	14	9.3	5.99	14.1	41.3	69.0	23.5	34.1	298	1.7
88A00028	M	1/1	14	18.1	6.29	14.3	43.0	68.4	22.7	33.3	497	2.2
88A00043	F	1/2	14	10.0	7.51	17.5	51.1	68.1	23.3	34.2	460	1.4
88A00047	F	1/2	14	11.5	6.79	15.8	46.4	68.4	23.3	34.1	323	4.2
Parameter means				12.23	6.65	15.43	45.45	68.48	23.20	33.93	394.5	2.38
Standard deviations				4.02	0.66	1.58	4.32	0.38	0.35	0.42	98.7	1.26
88A00037	M	2/1	14	10.4	6.42	15.0	45.3	70.6	23.4	33.1	313	1.9
88A00035	M	2/1	14	9.0	6.97	14.5	44.8	64.3	20.8	32.4	382	2.3
88A00044	F	2/2	14	8.6	7.02	16.5	48.8	69.5	23.5	33.8	265	2.9
88A00042	F	2/2	14	12.2	6.56	16.2	47.2	72.0	24.7	34.3	367	3.1
Parameter means				10.05	6.74	15.55	46.53	69.10	23.10	33.40	331.8	2.55
Standard deviations				1.63	0.30	0.95	1.84	3.36	1.64	0.83	53.5	0.55
88A00033	M	3/1	14	9.8	6.82	16.0	47.1	69.1	23.5	34.0	318	1.3
88A00031	M	3/1	14	11.1	7.00	15.8	48.4	69.1	22.6	32.6	310	2.7
88A00040	F	3/2	14	11.1	6.79	17.3	50.2	73.9	25.5	34.5	257	0.7
88A00046	F	3/2	14	9.6	5.72	13.9	39.8	69.6	24.3	34.9	296	0.7
Parameter means				10.41	6.58	15.75	46.38	70.43	23.98	34.00	295.3	1.35
Standard deviations				0.81	0.58	1.40	4.56	2.33	1.23	1.00	27.1	0.94

PRINTED: 22-Mar-89

ACUTE/ACUTE INTRAVENOUS

Study Start Date: 27-Sep-88

Animal Number	Sex	Group/ Subgroup	Day of Study	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT
88A00034	M	4/1	14	47	1	3	0.0	43	3	3	1	7.0	14.7
88A00029	M	4/1	14	31	0.0	10	0.0	57	2	0.0	3	9.0	17.7
88A00038	F	4/2	14	54	1	6	0.0	30	7	2	2	13.5	14.6
88A00041	F	4/2	14	43	0.0	6	0.0	44	5	2	0.0	7.4	15.0
Parameter means				43.8	0.5	6.3	0.0	43.5	4.3	1.8	1.5	9.23	15.50
Standard deviations				9.6	0.6	2.9	0.0	11.0	2.2	1.3	1.3	2.98	1.48
88A00032	M	1/1	14	62	0.0	1	0.0	31	6	0.0	0	7.0	22.5
88A00028	M	1/1	14	46	1	0.0	0	44	2	7	0.0	8.0	15.7
88A00043	F	1/2	14	47	0.0	2	0.0	37	7	7	3	9.2	16.8
88A00047	F	1/2	14	53	0.0	5	1	35	6	0.0	3	10.3	17.5
Parameter means				52.0	0.3	2.0	0.3	36.8	5.3	3.5	1.5	8.63	18.13
Standard deviations				7.3	0.5	2.2	0.5	5.4	2.2	4.0	1.7	1.43	3.01
88A00037	M	2/1	14	57	0.0	0	0.0	36	5	2	0.0	7.5	18.0
88A00035	M	2/1	14	32	1	4	0.0	47	7	9	0.0	8.2	15.0
88A00044	F	2/2	14	44	0.0	1	0.0	43	0.0	12	1	9.5	16.5
88A00042	F	2/2	14	38	0.0	3	0.0	51	7	1	0.0	8.8	15.7
Parameter means				42.8	0.3	2.0	0.0	44.3	4.8	6.0	0.3	8.50	16.30
Standard deviations				10.7	0.5	1.8	0.0	6.4	3.3	5.4	0.5	0.85	1.29
88A00033	M	3/1	14	50	0.0	9	0.0	30	9	2	1	8.0	15.0
88A00031	M	3/1	14	52	1	3	0.0	30	9	5	0.0	9.3	18.2
88A00040	F	3/2	14	42	1	1	0.0	49	6	1	1	9.5	17.0
88A00046	F	3/2	14	56	0.0	4	0.0	36	3	1	1	12.8	22.3
Parameter means				50.0	0.5	4.3	0.0	36.3	6.8	2.3	0.8	9.90	18.13
Standard deviations				5.9	0.6	3.4	0.0	9.0	2.9	1.9	0.5	2.04	3.08

Appendix I: PATHOLOGY REPORT

Principal Investigator: Denzil F. Frost, MS, DVM, CPT, VC
Co-Principal Investigator: Gary M. Zaucha, DVM, CPT, VC

I. INTRODUCTION

Study: Canine Acute Intravenous Toxicity Study.
Test Compound: Hypertonic Saline/Dextran 70®
Animal: *Canis familiaris*, Beagle, 6 months, Male and Female.
Dosage Groups: (20 ml/kg) MALE AND FEMALE
Group 1 Hypertonic Saline/Dextran 70®
Group 2 Hypertonic Saline
Group 3 Dextran 70®
Group 4 (Controls) Lactated Ringer's Solution

Reference: SOP-OP-STX-113

II. SUMMARY OF PROCEDURES

Euthanasia: Euthanol-6, IV.
Fixative: 10% Neutral Buffered Formalin.
Histopathology: Routine.
Clinical Lab: Hematology/Serology.

III. GROSS FINDINGS: Gross findings are summarized in Pathology Table 1. Two gross lesions were observed. In 88A00035 the lesion was multiple 1 mm diameter white spots (interpreted as cortical granulomas) bilaterally present in the kidneys. Microscopically, focal trace interstitial cortical fibrosis was observed, with trace multifocal nephrocalcinosis in the renal papilla. In 88A00041, marked otitis externa was observed grossly, but not examined microscopically.

IV: MICROSCOPIC FINDINGS: Tissues saved for microscopic examination from all groups were: brain, heart, lungs, spleen, liver with gall bladder, and kidneys.

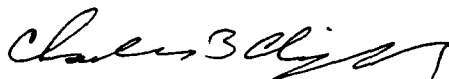
All tissues were examined in all groups.

Pathology Table 2 lists the incidence summary of all microscopic observations of all tissues from both sexes. Based on results of Kolmogorov-Smirnov two-tailed analysis (95% confidence level) of microscopic findings, no lesion was significantly more frequent in a treated group than in the control group, from either sex.

Appendix I (cont.): PATHOLOGY REPORT

The Pathology Annex contains the Individual Animal Reports, with gross and microscopic findings, for all animals.

V: SUMMARY COMMENTS: Lesions observed in these dogs were interpreted as incidental findings of little or no clinical significance. No morphologic evidence of toxicity due to the test compound was found.



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MAJ, VC
Diplomate, ACVP
Division of Pathology

Appendix I (cont.): PATHOLOGY REPORT

Glossary of Microscopic Findings

Brain

--Inflammation, Subacute: Aggregates of lymphocytes, with a few macrophages, in the neuropil.

Heart

--Arterial Intimal Proliferation: Thickening of the arterial wall by increased numbers of smooth muscle cells and/or fibroblasts.

Kidney

--Interstitial Cortical Fibrosis: Self-explanatory. May be accompanied by a few lymphocytes and/or plasma cells.

--Nephrocalcinosis: Small mineralized foci, often intratubular, are present in the renal papilla.

--Pyelitis, Subacute: Infiltration of the epithelium and subepithelial connective tissue of the renal pelvis with lymphocytes and neutrophils.

Liver

--Extramedullary Hematopoiesis: Small sinusoidal and occasionally periportal clusters of immature leukocytes and, occasionally, erythrocytes.

Lungs

--Inflammation, Subacute: Increased numbers of alveolar macrophages in alveoli surrounding respiratory bronchioles, with infiltration of local alveolar septa and peribronchiolar interstitial tissue with a mixed population of lymphocytes, plasma cells, and neutrophils.

Spleen

--Capsular Siderotic Plaque: Thickening and fibrosis of the splenic capsule accompanied by mineralization, accumulation of varying numbers of hemosiderin-laden macrophages, and occasionally extramedullary hematopoiesis.

Appendix I (cont.): PATHOLOGY REPORT

--Extramedullary Hematopoiesis: Small sinusoidal and occasionally periportal clusters of immature leukocytes and, occasionally, erythrocytes.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Incidence Summary Report for Gross Necropsy Observations
 Study Number: 88003
 Report includes all dead animals
 Study Start Date: 27-Sep-88

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 Page: 1

ACUTE/ACUTE INTRAVENOUS

	Males		Females		
	Ctls	Ctls	Ctls	Ctls	
	2	2	2	2	

EAR

OTITIS EXTERNA	0	0	0	0	1	0	0	0
Total:	0	0	0	0	1	0	0	0

KIDNEY

WMT.SPOTS(CORTICAL GRANULOMAS)	0	0	1	0	0	0	0	0
Total:	0	0	1	0	0	0	0	0

WHOLE BODY

NO GROSS LESIONS	2	2	1	2	1	2	2	2
Total:	2	2	1	2	1	2	2	2

Pathology Table 1

Appendix I (cont.): PATHOLOGY REPORT

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DOG/BEAGLE

Incidence Summary of Microscopic Observations
Study Number: 88003
All Diagnoses
Study Start Date: 27-Sep-88

PRINTED: 23-Mar-89
Page: 1

		.. Animals		A f f e c t e d ..	
		.. M a l e s F e m a l e s ..	
		Ctls	2	Ctls	2
T i s s u e s W i t h D i a g n o s e s		2	2	2	2
A n i m a l s e x :					
D o s a g e g r o u p :					
N o . i n g r o u p :					
N u m b e r e x a m i n e d :					
BRAIN	2	2	2	2	2
INFLAMMATION, SUBACUTE	0	0	0	0	0
HEART	2	2	2	2	2
ARTERIAL INTIMAL PROLIFERATION	0	0	0	0	0
KIDNEY	2	2	2	2	2
NEPHROCALCINOSIS	2	1	1	2	2
INTERSTITIAL CORTICAL FIBROSIS	0	0	1	0	0
PYELITIS, SUBACUTE	0	0	0	0	0
LIVER	2	2	2	2	2
EXTRAMEDULLARY HEMATOPOIESIS	2	2	2	0	1
LUNGS	2	2	2	2	2
INFLAMMATION, SUBACUTE	0	1	0	0	1
SPLEEN	2	1	2	2	2
EXTRAMEDULLARY HEMATOPOIESIS	1	1	2	1	2
CAPSULAR SIDEROTIC PLAQUE	0	0	0	0	0

Pathology Table 2

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00032 Sex: Male
 Day of death: 15 Status: Final sacrifice

Individual Animal Data Dump Table
 Study Number: 88003

Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Group: 1 Dose level: 20.00 ML/KG/day
 Terminal body weight (kms): 12.00

<< G r o s s O b s e r v a t i o n s >>
 Gross Free-Text Comments

Tissue Finding, severity NO GROSS LESIONS

WHOLE BODY

<< P a t h o l o g y O b s e r v a t i o n s >>
 Histopathologic diagnoses / Special histological comments

SPLEEN Required protocol tissue is missing.

LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

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Pathology Annex

Appendix I (cont.): PATHOLOGY REPORT

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DOG/BEAGLE

Individual Animal Data Dump Table
Study Number: 88003

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Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal: 88A00028

Sex: Male

Group: 1

Status: Final sacrifice

Dose level: 20.00 ML/KG/day

Terminal body weight (kms): 8.59

Day of death: 15

Gross Observations >>
Gross Free-Text Comments

Finding, severity

NO GROSS LESIONS

<< Pathology Observations >>

Tissue Histopathologic diagnoses / Special histological comments

LUNGS PNEUMONIA, SUBACUTE, Slight, Focal.

SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00037
 Day of death: 15

Sex: Male
 Status: Final sacrifice

Study Start Date: 27-Sep-88
 Group: 2

ACUTE/ACUTE INTRAVENOUS
 Dose level: 20.00 ML/KG/day
 Terminal body weight (kms): 12.00

Individual Animal Data Dump Table
 Study Number: 88003

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<< G r o s s O b s e r v a t i o n s >>
 Gross Free-Text Comments

Tissue Finding, severity
 WHOLE BODY NO GROSS LESIONS

<< P a t h o l o g y O b s e r v a t i o n s >>
 Histopathologic diagnoses / Special histological comments

Tissue
 SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, slight, focal.
 LIVER EXTRAMEDULLARY HEMATOPOIESIS, slight, focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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DOG/BEAGLE

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Individual Animal Data Dump Table
Study Number: 88003

Animal: 88A00035 Sex: Male Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Day of death: 15 Status: Final sacrifice Group: 2 Dose level: 20.00 ML/KG/day
Terminal body weight (kms): 12.45

Tissue Finding, severity << G r o s s O b s e r v a t i o n s >>
KIDNEY WHT.SPOTS(CORTICAL GRANULOMAS), Mild MULTIPLE 1MM DIA.WHT.SPOTS IN BOTH KID.

Tissue Histopathologic diagnoses / Special histological comments << P a t h o l o g y O b s e r v a t i o n s >>
SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.
INTERSTITIAL CORTICAL FIBROSIS, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00033 Sex: Male
 Day of death: 15 Status: Final sacrifice

Study Start Date: 27-Sep-88 Group: 3 Dose level: 20.00 ML/KG/day
 ACUTE/ACUTE INTRAVENOUS Terminal body weight (kms): 11.50

Tissue Finding, severity << G r o s s O b s e r v a t i o n s >>
 WHOLE BODY NO GROSS LESIONS Gross Free-Text Comments

Tissue << P a t h o l o g y O b s e r v a t i o n s >>
 SPLEEN Histopathologic diagnoses / Special histological comments
 EXTRAMEDULLARY HEMATOPOIESIS, Slight, focal.

LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
DOG/BEAGLE

Individual Animal Data Dump Table
Study Number: 88003

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Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal: 88A00031

Sex: Male

Status: Final sacrifice

Group: 3

Dose level: 20.00 ML/KG/day

Terminal body weight (kms): 10.81

Day of death: 15

Tissue Finding, severity
WHOLE BODY NO GROSS LESIONS

<< GROSS Observations >>
Gross Free-Text Comments

Tissue Histopathologic diagnoses / Special histological comments >>

SPLEEN

EXTRAMEDULLARY HEMATOPOIESIS, slight, focal.

LIVER

EXTRAMEDULLARY HEMATOPOIESIS, slight, focal.

KIDNEY

CALCIFICATION IN PAPILLA, slight, focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00034 Sex: Male
 Day of death: 15 Status: Final sacrifice

Individual Animal Data Dump Table
 Study Number: 88003

Study Start Date: 27-Sep-88 Group: 4 Dose level: 20.00 ML/KG/day
 ACUTE/ACUTE INTRAVENOUS Terminal body weight (kms): 9.86

Tissue Finding, severity << Gross Observations >>
 WHOLE BODY NO GROSS LESIONS Gross Free-Text Comments

Tissue Histopathologic diagnoses / Special histological comments << Pathology Observations >>
 SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
 LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
 KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
DOG/BEAGLE

Individual Animal Data Dump Table
Study Number: 88003

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Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal: 88A00029 Sex: Male
Status: Final sacrifice

Group: 4

Dose level: 20.00 ML/KG/day
Terminal body weight (kms): 10.97

Tissue Finding, severity << G r o s s O b s e r v a t i o n s >>
Gross Free-Text Comments

WHOLE BODY NO GROSS LESIONS

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue Histopathologic diagnoses / Special histological comments

LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00043 Sex: Female
 Day of death: 15 Status: Final sacrifice

Individual Animal Data Dump Table
 Study Number: 88003

Study Start Date: 27-Sep-88 Group: 1 Dose level: 20.00 ML/KG/day
 ACUTE/ACUTE INTRAVENOUS Terminal body weight (kms): 9.21

Tissue Finding, severity << G r o s s O b s e r v a t i o n s >>
 WHOLE BODY NO GROSS LESIONS Gross Free-Text Comments

Tissue Histopathologic diagnoses / Special histological comments << P a t h o l o g y O b s e r v a t i o n s >>
 LUNGS PNEUMONIA, SUBACUTE, Slight, Focal.

HEART ARTERIAL INTIMAL PROLIFERATION, Mild, Focal.

SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LEYTERMAN ARMY INSTITUTE OF RESEARCH		Individual Animal Data Dump Table		PRINTED: 23-Mar-89
DIV OF RES SUPP, PATH SERV GP		Study Number: 88003		Page: 10
PRESIDIO OF SAN FRANCISCO, CA 94129		Study Start Date: 27-Sep-88		
DOG/BEAGLE		ACUTE/ACUTE INTRAVENOUS		
Animal: 88A00047	Sex: Female	Group: 1	Dose level: 20.00 ML/KG/day	
Day of death: 15	Status: Final sacrifice		Terminal body weight (kms): 12.05	
Tissue	Finding, severity	<< G r o s s O b s e r v a t i o n s >>		
WHOLE BODY	NO GROSS LESIONS	Gross Free-Text Comments		
Tissue	<< P a t h o l o g y O b s e r v a t i o n s >>			
SPLEEN	Histopathologic diagnoses / Special histological comments			
LIVER	EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.			
KIDNEY	EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.			
	CALCIFICATION IN PAPILLA, Slight, Focal.			

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00044
 Day of death: 15
 Sex: Female
 Status: Final sacrifice

Individual Animal Data Dump Table
 Study Number: 88003
 Study Start Date: 27-Sep-88
 Group: 2
 Dose level: 20.00 ML/KG/day
 Terminal body weight (kms): 9.50
 ACUTE/ACUTE INTRAVENOUS

Tissue Finding, severity
 WHOLE BODY NO GROSS LESIONS

Tissue Necropsy memos
 No necropsy memos recorded on animal

Tissue Histopathologic diagnoses / Special histological comments
 SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
 LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
 KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

<< Gross Observations >>
 Gross Free-Text Comments

<< Necropsy Memos >>

<< Pathology Observations >>

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00042 Sex: Female
 Day of death: 15 Status: Final sacrifice

Individual Animal Data Dump Table
 Study Number: 88003

Study Start Date: 27-Sep-88 Group: 2 ACUTE/ACUTE INTRAVENOUS

Dose level: 20.00 ML/KG/day
 Terminal body weight (kms): 11.20

Tissue Finding, severity << G r o s s O b s e r v a t i o n s >>
 Gross Free-Text Comments

WHOLE BODY NO GROSS LESIONS

Tissue Histopathologic diagnoses / Special histological comments << P a t h o l o g y O b s e r v a t i o n s >>

BRAIN INFLAMMATION, SUBACUTE, Slight, Multifocal.

LUNGS PNEUMONIA, SUBACUTE, Slight, Focal.

SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.
 PYELITIS, SUBACUTE, Slight, Diffuse.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Individual Animal Data Dump Table
 Study Number: 88003
 Study Start Date: 27-Sep-88
 ACUTE/ACUTE INTRAVENOUS

Animal: 88A00040
 Sex: Female
 Status: Final sacrifice
 Day of death: 15
 Dose level: 20.00 ML/KG/day
 Terminal body weight (kms): 9.78

Group: 3
 Observations >>
 Gross Free-Text Comments

Tissue Finding, severity
 WHOLE BODY NO GROSS LESIONS

Tissue Histopathologic diagnoses / Special histological comments
 LUNGS PNEUMONIA, SUBACUTE, Slight, Focal.
 SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
 CAPSULAR SIDEROTIC PLAQUE, Slight, Multifocal.
 LIVER EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
 KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00046
 Day of death: 15
 Sex: Female
 Status: Final sacrifice

Individual Animal Data Dump Table
 Study Number: 88003

Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS

Dose level: 20.00 ML/KG/day
 Terminal body weight (kms): 12.10

Group: 3

Terminal body weight (kms): 12.10

Observations >>

Gross Free-Text Comments

NO GROSS LESIONS

NO GROSS LESIONS

Histopathologic diagnoses / Special histological comments

EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 DOG/BEAGLE

Animal: 88A00038 Sex: Female
 Day of death: 15 Status: Final sacrifice

Individual Animal Data Dump Table
 Study Number: 88003
 Study Start Date: 27-Sep-88

ACUTE/ACUTE INTRAVENOUS
 Dose level: 20.00 ML/KG/day
 Terminal body weight (kms): 10.60

Group: 4
 Observations >>
 Gross Free-Text Comments

Tissue Finding, severity << Pathology Observations >>
 WHOLE BODY NO GROSS LESIONS Histopathologic diagnoses / Special histological comments
 KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

Pathology Annex (cont.)

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF PES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
DOG/BEAGLE

Individual Animal Data Dump Table
Study Number: 88003

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Study Start Date: 27-Sep-88 ACUTE/ACUTE INTRAVENOUS

Animal: 88A00041 Sex: Female Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 10.77

Tissue Finding, severity << Gross Observations >>
..... Gross Free-text Comments
EAR OTITIS EXTERNA, Marked EXUDATE

Tissue << Pathology Observations >>
..... Histopathologic diagnoses / Special histological comments
SPLEEN EXTRAMEDULLARY HEMATOPOIESIS, Slight, Focal.
KIDNEY CALCIFICATION IN PAPILLA, Slight, Focal.

Pathology Annex (cont.)

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